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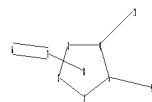
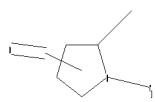
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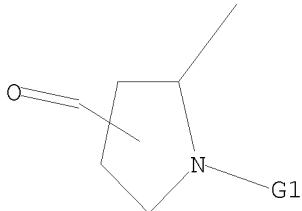
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ring nodes :  
1 2 3 4 5  
ring/chain nodes :  
11  
chain bonds :  
4-11 5-9 6-7  
ring bonds :  
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exact/norm bonds :  
1-2 1-5 2-3 3-4 4-5 5-9 6-7  
exact bonds :  
4-11
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G1:Cy,Hy

Match level :  
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS 11:Any

L1 STRUCTURE UPLOADED

=> d 11  
L1 HAS NO ANSWERS  
L1 STR



G1 Cy,Hy

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full

FULL SEARCH INITIATED 17:30:48 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 2432103 TO ITERATE

39.1% PROCESSED 950317 ITERATIONS

499 ANSWERS

41.1% PROCESSED 1000000 ITERATIONS  
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
SEARCH TIME: 00.00.28

535 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*INCOMPLETE\*\*  
BATCH \*\*INCOMPLETE\*\*

PROJECTED ITERATIONS: 2432103 TO 2432103

PROJECTED ANSWERS: 1193 TO 1409

L2 535 SEA SSS FUL L1

=> file cap1

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SINCE FILE ENTRY	TOTAL SESSION
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=> s 12

L3

73 L2

=> d 13 53-73 ibib abs hitstr

L3 ANSWER 53 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:582909 CAPLUS

DOCUMENT NUMBER: 141:218310

TITLE: Insights into Phenylalanine Derivatives Recognition of VLA-4 Integrin: From a Pharmacophoric Study to 3D-QSAR and Molecular Docking Analyses

AUTHOR(S): Macchiarulo, Antonio; Costantino, Gabriele; Meniconi, Mirco; Pleban, Karin; Ecker, Gerhard; Bellocchi, Daniele; Pellicciari, Roberto

CORPORATE SOURCE: Dipartimento di Chimica e Tecnologia del Farmaco, Universita di Perugia, Perugia, 06127, Italy

SOURCE: Journal of Chemical Information and Computer Sciences (2004), 44(5), 1829-1839

CODEN: JCISD8; ISSN: 0095-2338

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The very late antigen-4 (VLA-4), also known as integrin  $\alpha 4\beta 1$ , is expressed on monocytes, T- and B-lymphocytes, basophils, and eosinophils and is involved in the massive recruitment of granulocytes in different pathol. conditions such as multiple sclerosis and asthma. VLA-4 interacts with its endogenous ligand VCAM-1 during chronic inflammation, and blockade of VLA-4 /VCAM-1 interaction is a potential target for immunosuppression. Two classes of VLA-4 antagonists have so far been reported:  $\beta$ -amino acid derivs. containing a diaryl urea moiety (BIO-1211) and phenylalanine derivs. (TR-14035). With the aim of clarifying the structural basis responsible for VLA-4 recognition by phenylalanine derivs., the authors developed a combined computational study on a set of 128 antagonists available through the literature. Our computational approach is composed of three parts. (i) A VCAM-1 based pharmacophore was constructed with a restricted number of phenylalanine derivs. to identify the region of the protein that resembles synthetic antagonists. The pharmacophore was instrumental in constructing an alignment of a set of 128 compds. This alignment was exploited to build a pseudoreceptor model with the RECEPTOR program. (ii) 3D-QSAR anal. was carried out on the computed electrostatic and steric interaction energies with the pseudoreceptor surface. The 3D-QSAR anal. yielded a predictive model able to explain much of the variance of the 128 antagonists. (iii) A homol. modeling study of the headpiece of VLA-4 based on the crystal structure of  $\alpha\beta 3$  was performed. Docking expts. of TR-14035 into the binding site of VLA-4 aided the interpretation of the 3D-QSAR model. The obtained results will be fruitful for the design of new potent and selective antagonists of VLA-4.

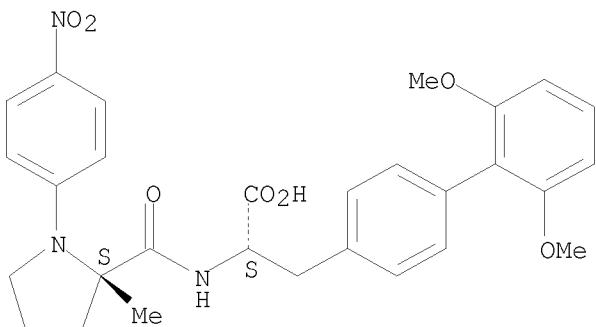
IT 737804-72-7

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(3D-QSAR and mol. docking analyses of phenylalanine derivs. recognition of VLA-4 integrin)

RN 737804-72-7 CAPLUS

CN L-Alanine, 2-methyl-1-(4-nitrophenyl)-L-prolyl-3-(2',6'-dimethoxy[1,1'-biphenyl]-4-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 54 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1966:59736 CAPLUS

DOCUMENT NUMBER: 64:59736

ORIGINAL REFERENCE NO.: 64:11149g-h,11150a-e

TITLE: 1,3-Cycloadditions of azomethinylides from aziridinecarboxylic esters

AUTHOR(S): Huisgen, Rolf; Scheer, Wolfgang; Szeimies, Guenter; Huber, Helmut

CORPORATE SOURCE: Univ. Munich, Germany

SOURCE: Tetrahedron Letters (1966), (4), 397-404

CODEN: TELEAY; ISSN: 0040-4039

DOCUMENT TYPE: Journal

LANGUAGE: German

GI For diagram(s), see printed CA Issue.

AB cf. Heine and Peavy, CA 63, 14796e. By a ring opening between the 2 and 3 positions, di-Me 1-(p-methoxyphenyl)aziridine-2,3-dicarboxylate (I) adds to C:C and C.tplbond.C compds. to give pyrrolidine or pyrroline derivs.

Heating di-Me 1-(p-methoxyphenyl)-Δ2-1,2,3-triazoline-4,5-trans-dicarboxylate at 100° gives I as a 15:85 cis-trans mixture. The reactions and epimerizations of I presumably proceed through the intermediate formation of epimers of MeO2CCH: N+(p-MeOC6H4)C-HCO2Me. Heating di-Me fumarate (II) and I at 140° yields 94% tetra-Me 1-(p-methoxyphenyl)pyrrolidine-2,3,4,5-tetracarboxylate (III) containing an oily isomer (IIIa) and 59% of a crystalline isomer (IIIb), m. 112-13°. IIIa and IIIb are dehydrogenated by chloranil (IV) in boiling Decalin to give 21 and 22% yields, resp., of tetra-Me 1-(p-methoxyphenyl)pyrrole-2,3,4,5-tetracarboxylate, independently synthesized by the method of Huntress, et al. (CA 50, 12977b) from p-MeOC6H4NHOH and (MeO2CC.tplbond.)2. III is also prepared in 61% yield from II and p-MeOC6H4N3 at 100-140°. At 120°, I and [(EtO2C)2CH:]2 give 77% of 2,5-di-Me 3,3,4,4-tetra-Et 1-(p-methoxyphenyl)pyrrolidine-2,3,3,4,4,5-hexacarboxylate containing 65% of the cis form, m. 114-15°, and 35% of the trans form, m.

114-16°, separated on silica gel by 9:1 C6H6-Et2O. The addition of norbornene to I at 100° gives 94% V containing 63% cis form (V, R = CO2Me, R1 = H), an oil, and 37% trans form (V, R = H, R1 = CO2Me), m. 87-9°, separated by thin layer chromatography. IV in boiling cymene converts V to VI, m. 161-2°. At 125°, I combines with HC.tplbond.CH in Me2CO to give an 81% yield of adducts, presumably a mixture of Δ2- and Δ3-pyrrolines which are dehydrogenated by IV in boiling xylene to give a 68% yield of di-Me 1-(p-methoxyphenyl)pyrrole-2,5-dicarboxylate, identical to the product obtained from p-MeOC6H4NH2 and di-Me α,α'-dihydroxymuconate (Kuhn and Dury, CA 45, 7017a).

BzC.tplbond.CPh and I at 100° yield 93% of an adduct dehydrogenated by IV in PhMe to give 55% di-Me ester of 3-benzoyl-1-(p-methoxyphenyl)-4-

phenylpyrrole-2,5-dicarboxylic acid (VII). VII decarboxylates at 200° to give 3-benzoyl-1-(4-methoxyphenyl)-4-phenylpyrrole (VIII), characterized by its 2,4-dinitrophenylhydrazone. VIII is also prepared by condensing the Na derivative of BzCH<sub>2</sub>CHO with p-MeOC<sub>6</sub>H<sub>4</sub>NHCH<sub>2</sub>Bz, and cyclizing the product with concentrated H<sub>2</sub>SO<sub>4</sub>. Photochem. or thermally (150°), I dimerizes to give a mixture from which two isomers, m. 188-9° and 240-1°, of tetra-Me 1,4-bis(p-methoxyphenyl)piperazine-2,3,5,6-tetracarboxylate have been isolated. Heating Me 1-phenylaziridine-2-carboxylate (IX) 6 hrs. at 200° gave 50% of the di-Me ester of 1,4-diphenylpiperazine-2,3-trans-dicarboxylic acid (X), m. 132-3°, and 5% of the cis ester, m. 105-6°. Distillation of Ca salt of X yields (PhNHCH<sub>2</sub>)<sub>2</sub> and 1,4-diphenylpiperazine. The reaction of IX with trans-(BzCH<sub>2</sub>)<sub>2</sub> (XI) gives a 1:1 adduct, m. 120-1°, and with PhCH<sub>2</sub>NMe, an adduct, m. 132.5-4° (structures not given). The addition of 1-benzyl-2,3-trans-dibenzoylaziridine to XI gives 34% of 1-benzyl-2,3,4,5-(all-trans)-tetrabenzoylpyrrolidine.

IT 875613-01-7P, 4,7-Methanoisoindoline-1,3-dicarboxylic acid, hexahydro-2-(p-methoxyphenyl)-, dimethyl ester, cis-

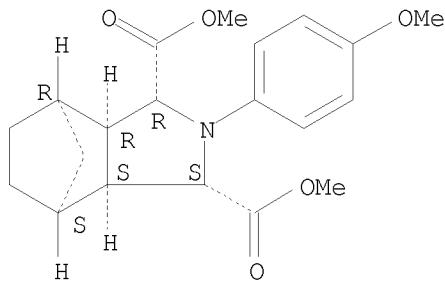
RL: PREP (Preparation)

(preparation of)

RN 875613-01-7 CAPLUS

CN INDEX NAME NOT YET ASSIGNED

Relative stereochemistry.



L3 ANSWER 55 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1956:64500 CAPLUS

DOCUMENT NUMBER: 50:64500

ORIGINAL REFERENCE NO.: 50:12020g-i

TITLE: Synthesis of spasmolytic substances. X. Synthesis of some alkylamino esters of pyrrolidine-2,5-dicarboxylic acid

AUTHOR(S): Klosa, Josef

SOURCE: Arch. Pharm. (1955), 288, 72-4

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

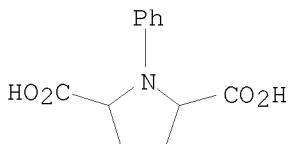
AB cf. C.A. 49, 8274d. Adipic acid (100 g.) and 200 cc. SOCl<sub>2</sub> heated 2 hrs. on the steam bath, the volatile products removed in vacuo, the residual oily product brominated at 50° under ultraviolet light with 200 g. of Br and the product allowed to stand 24 hrs. with 700 cc. absolute EtOH gave 90 g. di-Et 2,5-dibromoadipate (I), m. 65-7° (from benzene). Di-Me 2,5-dibromoadipate, prepared similarly, m. 75-7°. I (10 g.) and 30 g. aniline refluxed 18 hrs. in 100 cc. benzene, and fractionally distilled gave 7 g. di-Et 1-phenyl-2,5-pyrrolidinedicarboxylate (II), b<sub>2</sub> 230-40°. The di-Me ester, b<sub>2</sub> 250-60°, m. 85-7°, and di-Et 1-butyl-2,5-pyrrolidinedicarboxylate, b<sub>2</sub> 156-8°, were prepared similarly. II (20 g.) refluxed 24 hrs. with 100 g. Et<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>OH, and the mixture fractionally distilled gave 12 g. of 1-phenyl-2,5-pyrrolidinedicarboxylic acid di(β-diethylaminoethyl) ester, b<sub>1</sub>

193-5°. The following di( $\beta$ -diethylaminoethyl) esters of 2,5-pyrrolidinedicarboxylic acid were prepared similarly: 1-butyl, 60%, b1 168-9°; 1-methyl, 43%, b1 174-7°; 1-benzyl, 52%, b1 200-3°; and 1-propyl, 35%, b1 167-70°.

IT 859957-82-7, 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl-(esters)

RN 859957-82-7 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl- (CA INDEX NAME)



L3 ANSWER 56 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1956:20042 CAPLUS

DOCUMENT NUMBER: 50:20042

ORIGINAL REFERENCE NO.: 50:4125d-i, 4126a-b

TITLE: 2,3-Pyrrolidinediones. IV. Further studies on tautomerism

AUTHOR(S): Vaughan, Wyman R.; McCane, Donald I.

CORPORATE SOURCE: Univ. of Michigan, Ann Arbor

SOURCE: Journal of Organic Chemistry (1955), 20, 143-54  
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 50:20042

AB cf. C.A. 48, 3340i. Addnl. evidence has been presented that 1,5-diaryl-2,3-pyrrolidinediones are tautomeric with  $\alpha$ -arylimino- $\beta$ -arylidenepropionic acids and that it is the latter which undergo thermal decarboxylation. Refluxing 14.4 g. 1,4-diphenylazetidinone overnight in 125 cc. MeOH saturated with HCl, evaporating the mixture in vacuo, and

treating the residue with H<sub>2</sub>O and a little NaHCO<sub>3</sub> give 86.5% Me  $\beta$ -phenyl- $\beta$ -phenylaminopropionate, needles, m. 105-6°, which (5.1 g.) is treated in 50 cc. dry (CH<sub>2</sub>Cl)<sub>2</sub> containing 15 cc. C<sub>5</sub>H<sub>5</sub>N 3 hrs. at 20° with 3 cc. MeO<sub>2</sub>CCOCl, the mixture is diluted with 50 cc. Et<sub>2</sub>O, and the residue of the washed (H<sub>2</sub>O, 5% HCl-H<sub>2</sub>O) and dried Et<sub>2</sub>O solution evaporated, giving 95% Me  $\beta$ -phenyl- $\beta$ -(N-methoxallyl-N-phenylamino)-propionate (I), m. 75.5-6°. Adding MeONa (from 0.07 g. Na) in 20 cc. absolute MeOH to 0.9 g. I, keeping the mixture 4 hrs., neutralizing it with the calculated amount of AcOH in 50 cc. H<sub>2</sub>O, and extracting with Et<sub>2</sub>O give 0.5 g.

4-carbomethoxy-1,5-diphenyl-2,3-pyrrolidinedione (II), m. 196-9° (decomposition); it gives a deep red color with FeCl<sub>3</sub>. Adding 2 g. Me methoxallylacetate to 50 cc. Et<sub>2</sub>O containing 2 g. PhCH:NPh and evaporating the filtered solution give II. Refluxing a sample of the Et ester of II in PhNO<sub>2</sub> gives 1 mole CO<sub>2</sub> and 1,5-diphenyl-2,3-pyrrolidinedione (III). Heating 22.5 g. CuC<sub>14</sub>N with 37 g. AcBr 2 hrs. at 70-80° gives 54.3% MeCOC<sub>14</sub>N, b. 87-91°, which (9 g.) is treated at 0° with 12.5 cc. concentrated HCl, and the mixture diluted with 40 cc. H<sub>2</sub>O and heated 2 hrs. at

70°, giving 38% MeCOC<sub>14</sub>O<sub>2</sub>H (IV), b<sub>18</sub> 40-60°. Adding 1 g. IV to 5 cc. 10% NaOH, then adding at 0° 1.2 g. BzH and, dropwise (10 min.), 3 cc. 10% NaOH, and stirring the mixture 50 min. with the temperature kept

below 12° give 0.9 g. PhCH:CHCOC<sub>14</sub>O<sub>2</sub>Na which, dissolved in 20 cc. ice H<sub>2</sub>O, is decomposed with 25 drops concentrated HCl in 10 cc. ice-H<sub>2</sub>O, giving

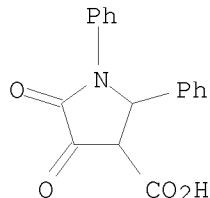
47% PhCH: CHCOC<sub>14</sub>O<sub>2</sub>H (V), m. 68-9°. Adding 0.36 g. PhNH<sub>2</sub> in 5 cc. absolute EtOH dropwise to 0.67 g. V in 15 cc. absolute EtOH, stirring the mixture

0.5 hr. at 20°, diluting it with 25 cc. EtOH, and refluxing it 1 hr. give 80% III-2-C<sub>14</sub> (VI), m. 158-60° (decomposition). o-C<sub>6</sub>H<sub>4</sub>(CO)N<sub>15</sub>H is converted into PhN<sub>15</sub>H<sub>2</sub> which, with PhCH:CHCOCO<sub>2</sub>H, gives III-1-N<sub>15</sub> (VII). Refluxing 2.51 g. VII in 25 cc. absolute EtOH 0.5 hr. with 1.1 g. PhNHNH<sub>2</sub> in 10 cc. absolute EtOH and 4 drops AcOH, keeping the mixture 12 hrs. at 20%, refluxing it another hr., and diluting the cooled solution with 70 cc. H<sub>2</sub>O give 79% inactive 1-anilino-5-phenyl-2,3-pyrrolidinedione (VIII), m. 154-5° (decomposition); the mother liquor is extracted with C<sub>6</sub>H<sub>6</sub> and HCl is passed into the extract, giving PhN<sub>15</sub>H<sub>2</sub>.HCl (IX). Treating III with PhNHNH<sub>2</sub> (X) (prepared from PhNH<sub>2</sub> and KN<sub>15</sub>O<sub>3</sub>) gives 75% active VIII, m. 154.5-6° (decomposition). For the collecting of N for mass spectrometric analysis 0.39 g. PhNH<sub>2</sub>.HCl, 6 g. 50% H<sub>3</sub>PO<sub>2</sub>, and 10 cc. H<sub>2</sub>O are treated at 5° with 0.21 g. NaNO<sub>2</sub> in 10 cc. H<sub>2</sub>O. The decarboxylation of VI is carried out by heating 0.251 g. in 20 cc. o-C<sub>6</sub>H<sub>4</sub>Cl<sub>2</sub> 1 hr. at 180° (bath temperature), absorbing the CO<sub>2</sub> in 1N NaOH by means of a CO<sub>2</sub>-free N stream, and precipitating it as BaCO<sub>3</sub>. This gives BaC<sub>14</sub>O<sub>3</sub> with 94.9% of the starting C<sub>14</sub>, indicating that VI is thermally decarboxylated to cinnamylideneaniline and C<sub>14</sub>O<sub>2</sub> by initial rearrangement to the isomeric 3-arylidene-2-aryliminopropionic acids. In the reaction of III with X active VIII is formed by an exchange between tautomeric arylimino acid and X.

IT 873399-08-7, 3-Pyrrolidinecarboxylic acid, 4,5-dioxo-1,2-diphenyl-  
(esters)

RN 873399-08-7 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4,5-dioxo-1,2-diphenyl- (CA INDEX NAME)



L3 ANSWER 57 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1955:46203 CAPLUS

DOCUMENT NUMBER: 49:46203

ORIGINAL REFERENCE NO.: 49:8908f-i,8909a-b

TITLE: Pyrrolidine esters

AUTHOR(S): Van Heyningen, Earle M.

CORPORATE SOURCE: Eli Lilly & Co., Indianapolis, IN

SOURCE: Journal of the American Chemical Society (1954), 76, 3043-4

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 49:46203

AB The condensation of 1,3-dibromoalkanes with an aminomalonate in refluxing EtOH with NaOEt yielded the corresponding 2,2-dialkoxyprrolidines in fair yields. The yields could be improved considerably by effecting the cyclization in a nonhydroxylic solvent using NaNH<sub>2</sub>. Na (14.1 g.) dissolved in 350 cc. absolute EtOH, the solution treated with 107 g. H<sub>2</sub>NCH(CO<sub>2</sub>Et)<sub>2</sub> and then with 246.5 g. Br(CH<sub>2</sub>)<sub>3</sub>Br in large portions, the mixture refluxed 4 hrs., the EtOH removed in vacuo, the residue dissolved in dilute HCl, the acid solution extracted with Et<sub>2</sub>O to recover the unreacted Br(CH<sub>2</sub>)<sub>3</sub>Br (90 g.), basified with dilute aqueous NaOH, and extracted with Et<sub>2</sub>O, and

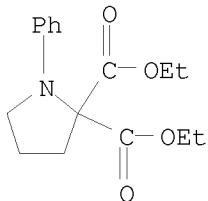
the extract dried and distilled yielded 28.8 g. (22%) 2,2-dicarbethoxypyrrolidine (II), b2 105°, n25D 1.4455. II in Et2O treated with dry HCl gave II.HCl, white needles, m. 91-2° (from Et2O-CHCl3). I (135.5 g.) and then 357 g. (MeCHBr)2CH2 (III) added to 18 g. Na in 450 cc. absolute EtOH, and the mixture refluxed 12 hrs. and worked up in the usual manner gave 250 g. recovered III and 66.3 g. (35.6%) 3,5-di-Me derivative (IV) of II, b1 91-4°, n25D 1.4447. NaNH2 prepared from 36 g. Na in 1 l. liquid NH3, the NH3 evaporated and replaced by 500 cc. dry C6H6 which was refluxed to remove traces of NH3, the mixture treated with 136.7 g. I, gently warmed to remove all of the NH3 while being bubbled with dry N, treated dropwise with stirring with 200 g. III, refluxed 26 hrs., cooled, diluted with H2O, and extracted with C6H6, and the extract washed and distilled yielded 128.2 g. (67.7%) IV, b0.76 89-93°, n25D 1.4455. IV in dry Et2O treated with dry HCl gave IV.HCl, m. 105-7° (from CHCl3-Et2O). IV (66.3 g.) added to a suspension of NaNH2 (from 6.45 g. Na in liquid NH3) in 200 cc. PhMe, and the mixture heated 15 hrs. and worked up in the usual manner gave 29.8 g. (42.5%) IV, b0.8-1.1 99-105°, n25D 1.4515. NaNH2 (from 4.6 g. Na) suspended in 200 cc. PhMe and treated with 25.3 g. PhNHCH(CO2Et)2, the NH3 removed, the residual mixture treated with 20.1 g. Br(CH2)3Br and refluxed gave similarly 8.0 g. (27.5%) 1-Ph derivative of II, b0.6 145°, n25D 1.5132. NaNH2 (from 27.6 g. Na) suspended in 700 cc. PhMe treated with 100 g. NC(AcNH)CHCO2Et, the NH3 removed, and the mixture treated with 121.5 g. Br(CH2)3Br and worked up in the usual manner yielded 54.0 g. (43.5%) 1-acetyl-2-carbethoxy-2-cyanopyrrolidine (V), b1 163°, n25D 1.4765. V (15 g.) refluxed 8 hrs. with 9.65 g. guanidine carbonate in EtOH containing NaOEt, and the liquid mixture decanted into H2O gave 9 g. spiro[1-acetylpyrrolidine-2,5'-(2,4-diiminobarbituric acid)], m. 311-12° (from H2O).

IT 860360-20-9P, 2,2-Pyrrolidinedicarboxylic acid, 1-phenyl-, diethyl ester

RL: PREP (Preparation)  
(preparation of)

RN 860360-20-9 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-phenyl-, 2,2-diethyl ester (CA INDEX NAME)



L3 ANSWER 58 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1954:60443 CAPLUS

DOCUMENT NUMBER: 48:60443

ORIGINAL REFERENCE NO.: 48:10733g-i,10734a-i,10735a-b

TITLE: The condensation of oxalic esters with esters of β-alanine and N-substituted 3-aminopropionic acids. Synthesis of some derivatives of 2,3-dioxopyrrolidine and 2-oxo-3-methoxy-3-pyrroline Southwick, Philip L.; Crouch, Robert T.

AUTHOR(S): Carnegie Inst. of Technol., Pittsburgh, PA

CORPORATE SOURCE: Journal of the American Chemical Society (1953), 75, 3413-17

SOURCE: CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable  
OTHER SOURCE(S): CASREACT 48:60443  
AB The condensation of (CO<sub>2</sub>Me)<sub>2</sub> or (CO<sub>2</sub>Et)<sub>2</sub> with a series of N-substituted 3-aminopropionic acid esters yielded a series of 1-substituted 4-carbomethoxy- and 4-carbethoxy-2,3-dioxopyrrolidines (I), converted into 4-carbalkoxy-2-oxo-3-methoxy-3-pyrrolines by treatment with CH<sub>2</sub>N<sub>2</sub>. The 4-carbalkoxy-1-benzyl-2,3-dioxopyrrolidines were hydrolyzed and decarboxylated to 1-benzyl-2,3-dioxopyrrolidine (II). Cyclohexylamine (49.5 g.) and 43 g. freshly distilled CH<sub>2</sub>:CHCO<sub>2</sub>Me (III) in 400 cc. absolute MeOH let stand 24 hrs., the solvent distilled off, and the residual oil fractionated gave 83 g. (90%) Me 3-(cyclohexylamino)propionate, b<sub>4</sub>-5 125-8°, giving in dry C<sub>6</sub>H<sub>6</sub> with dry HCl the HCl salt, white needles, m. 163-4° (from MeOH). Similarly was prepared the corresponding Et ester (IV), b<sub>3</sub>-5 133-5°, 85%; [HCl salt, colorless needles, m. 145-6° (from absolute EtOH)], and Me 3-(benzylamino)propionate (V), b<sub>7</sub> 145-7° 92%; [HCl salt, white plates, m. 164-5° (from MeOH)]. p-MeC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> (35.3 g.), 28.4 g. III, 40 cc. dry C<sub>6</sub>H<sub>6</sub>, and 10 drops SnCl<sub>4</sub> refluxed 24 hrs. yielded 42.5 g. (67%) p-MeC<sub>6</sub>H<sub>4</sub>NH(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>Me, b<sub>5</sub>-6 145-50°, m. 60-1°, light yellow plates from C<sub>6</sub>H<sub>6</sub>-petr. ether. p-MeC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> (53.5 g.), 50 g. freshly distilled CH<sub>2</sub>:CHCO<sub>2</sub>Et, and 20 g. glacial AcOH refluxed 24 hrs., and the resulting deep red solution distilled gave 52 g. (50%) p-MeC<sub>6</sub>H<sub>4</sub>NH(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>Et, b<sub>2</sub>-3 142-4°; HCl salt, white needles, m. 92-3° (from absolute EtOH). Similarly was prepared PhNH(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>Et, 63%, b<sub>1</sub>-2 139-46°; HCl salt, m. 98-9°. To 5.4 g. NaOMe in 50 cc. dry Et<sub>2</sub>O was added with stirring 11.8 g. (CO<sub>2</sub>Me)<sub>2</sub> and then 19.3 g. V in 50 cc. Et<sub>2</sub>O, the mixture refluxed 0.5 hr. with stirring, the Et<sub>2</sub>O distilled off, the residual salt taken up in 500 cc. warm H<sub>2</sub>O, the mixture acidified with dilute HCl, let stand several hrs., filtered, and the residue recrystd. from MeOH to yield 18 g. (75%) 4-carbomethoxy-1-benzyl-2,3-dioxopyrrolidine (VI), white needles, m. 180-2° [recrystd., m. 183-4° (from MeOH)]. Similarly were prepared the following 1-substituted-4-carbomethoxy-2,3-dioxopyrrolidines (1-substituent, % yield, and m.p. given): p-MeC<sub>6</sub>H<sub>4</sub>, colorless needles, 45, 193-4° (from MeOH); m-C<sub>1</sub>C<sub>6</sub>H<sub>4</sub>, colorless needles, 29, 185-6° (from MeOH); p-MeOC<sub>6</sub>H<sub>4</sub>, yellow needles, 30, 209-10° (from MeOH); cyclohexyl, colorless needles, 29, 178-9° (from MeOH); and 1-phenyl-4-carbethoxy-2,3-dioxopyrrolidine, colorless needles, 48, 153° (from EtOH). Et 3-(cyclohexylamino)propionate (19.9 g.) and 14.6 g. (CO<sub>2</sub>Et)<sub>2</sub> refluxed 1 hr. on the steam bath with 6.8 g. NaOEt, the resulting solid filtered off, washed with Et<sub>2</sub>O, suspended in 500 cc. warm H<sub>2</sub>O, acidified, let stand several hrs., filtered, and the filter residue recrystd. from 95% EtOH yielded 16.5 g. (65%) 1-cyclohexyl-4-carbethoxy-2,3-dioxopyrrolidine, white needles, m. 185-6° (recrystd., m. 188°). Similarly were prepared the following 1-substituted-4-carbethoxy-2,3-dioxopyrrolidines (1-substituent, % yield, and m.p. given): p-MeC<sub>6</sub>H<sub>4</sub> (VII), colorless needles, 52, 156° (from EtOH); m-C<sub>1</sub>C<sub>6</sub>H<sub>4</sub>, colorless needles, 37, 142-3° (from EtOH); p-MeOC<sub>6</sub>H<sub>4</sub>, yellow needles, 55, 160-1° (from EtOH); and PhCH<sub>2</sub>, (VIII), colorless needles, 75, 135-6° (from EtOH). PhNH(Ph)CHCH<sub>2</sub>CO<sub>2</sub>Et (10.3 g.) and 6.1 g. (CO<sub>2</sub>Et)<sub>2</sub> in 25 cc. absolute EtOH added to 2.8 g. NaOEt in 50 cc. absolute EtOH, the EtOH distilled off on the steam bath, the light tan liquid residue dissolved in 300 cc. warm H<sub>2</sub>O, the solution acidified with 20% HCl, and the light tan solid precipitate recrystd. from EtOH gave 9 g. (73%) 4-carbethoxy-1,5-diphenyl-2,3-dioxopyrrolidine, white needles, m. 172-4°. Similarly was prepared 4-carbethoxy-2,3-dioxopyrrolidine, white plates, 72%, m. 185-6° (from EtOH) preheated to 175°. VII (2 g.) in 10 cc. Et<sub>2</sub>O treated with excess CH<sub>2</sub>N<sub>2</sub> in Et<sub>2</sub>O, the excess CH<sub>2</sub>N<sub>2</sub> destroyed with AcOH, the Et<sub>2</sub>O evaporated, and the residual light yellow oil recrystd. from EtOH gave 2 g.

(95%) 4-carbethoxy-1-p-tolyl-3-methoxy-2-oxo-3-pyrroline, colorless needles, m. 82-3° (from EtOH). Similarly were prepared the following 1-substituted-4-carbethoxy-2-oxo-3-methoxy-3-pyrrolines (1-substituent, % yield, and m.p. given): m-ClC<sub>6</sub>H<sub>4</sub>, colorless needles, 91, 140-1° (from EtOH); p-MeOC<sub>6</sub>H<sub>4</sub>, colorless needles, 95, 109-10° (from EtOH); cyclohexyl, colorless needles, 91, 86-7° (from EtOH); Ph, colorless needles, 95, 76-7° (from EtOH); H, colorless needles, 74, 105-6° (from MeOH); and the following 1-substituted-4-carbomethoxy-2-oxo-3-methoxy-3-pyrrolines: p-MeC<sub>6</sub>H<sub>4</sub>, colorless needles, 95, 141-2° (from MeOH); m-ClC<sub>6</sub>H<sub>4</sub>, colorless needles, 86, 115-16° (from MeOH); p-MeOC<sub>6</sub>H<sub>4</sub>, light yellow needles, 94, 133-4° (from MeOH); cyclohexyl, colorless needles, 95, 103-4° (from MeOH); PhCH<sub>2</sub>, colorless needles, 95, 77-8° (from MeOH).

Ph(MeO<sub>2</sub>CO)NCH(Ph)CH<sub>2</sub>CO<sub>2</sub>Me (5 g.) in 50 cc. dry MeOH treated with 0.81 g. NaOMe in 25 cc. MeOH, and the precipitated white gelatinous Na salt filtered off

and triturated with AcOH gave 1 g. PhNHCOCO<sub>2</sub>Me, m. 111-12°; the filtrate from the Na salt evaporated to dryness, the residual solid extracted with

H<sub>2</sub>O, the aqueous extract acidified, and the resulting precipitate recrystd. from MeOH

gave 0.4 g. (9%) 4-carbomethoxy-1,5-diphenyl-2,3-dioxopyrrolidine, m. 199-200°; the residue (0.3 g.) from the H<sub>2</sub>O extraction was PhCH:CHCO<sub>2</sub>Me, m. 32-3°. VIII (2 g.) and 150 cc. 20% HCl refluxed 3 hrs., the mixture cooled, filtered, extracted several times with CHCl<sub>3</sub>, the CHCl<sub>3</sub> evaporated,

and the light tan oily residue crystallized from C<sub>6</sub>H<sub>6</sub> gave 1.2 g. (83%) 1-benzyl-2,3-dioxopyrrolidine, white needles, m. 99-100°, also obtained in 69% yield from VI by a similar hydrolysis. PhCH<sub>2</sub>NH(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>Et (30 g.) and 150 cc. 10% NaOH refluxed until the ester layer disappeared, the solution neutralized with dilute HCl, evaporated to dryness, the white solid

residue extracted with boiling absolute EtOH, and the extract cooled gave 22.5 g.

(87%) PhCH<sub>2</sub>NH(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H (IX), white needles, m. 182-3°. IX (5 g.) and 10 g. MeO<sub>2</sub>CCOCl heated 0.5 hr. on the steam bath, the solution diluted with 100 cc. Et<sub>2</sub>O, washed with H<sub>2</sub>O, extracted with excess 5% aqueous NaHCO<sub>3</sub>, the alkaline

extract acidified, the precipitated light yellow oil let stand, and the resulting

solid recrystd. from CHCl<sub>3</sub>-petr. ether yielded 5 g. (68%) Ph-CH<sub>2</sub>N(COCO<sub>2</sub>Me)CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H (X), white plates, m. 99-100°. X (8 g.) and 8 g. MeO<sub>2</sub>CCOCl in 25 cc. anhydrous CHCl<sub>3</sub> treated with 8 g. pyridine, the solution let stand 2 hrs., washed with H<sub>2</sub>O, heated on the steam bath with 400 cc. 5% aqueous NaHCO<sub>3</sub>, the aqueous extract decolorized with C, filtered, the filtrate

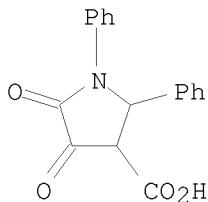
acidified, an unidentified precipitated acid (XI) (2.2 g.) filtered off, the filtrate extracted with CHCl<sub>3</sub>, and the extracted evaporated gave 0.5 g. 1-benzyl-2-oxo-3-methoxy-3-pyrroline-4-carboxylic acid, m. 139-40° (from CHCl<sub>3</sub>-petr. ether), esterified with CH<sub>2</sub>N<sub>2</sub> to VI, m. 77-8°.

XI dissolved in aqueous KOH, repptd. with HCl, and recrystd. from aqueous EtOH gave small pale yellow plates, m. 245-6°.

IT 873399-08-7, 3-Pyrrolidinecarboxylic acid, 4,5-dioxo-1,2-diphenyl- (esters)

RN 873399-08-7 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4,5-dioxo-1,2-diphenyl- (CA INDEX NAME)



L3 ANSWER 59 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1953:25510 CAPLUS

DOCUMENT NUMBER: 47:25510

ORIGINAL REFERENCE NO.: 47:4373g-i, 4374a-e

TITLE: Amino esters of 1-substituted 2,5-pyrrolidinedicarboxylic acids

INVENTOR(S): Hill, Arthur J., Jr.; Maynard, John T.

PATENT ASSIGNEE(S): American Cyanamid Co.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2596099		19520513	US 1946-719108	19461228

AB Dialkyl dibromo adipates with primary amines give esters of 1-substituted 2,5-pyrrolidinedicarboxylic acids, and the products undergo ester interchanges with tertiary amino alcs. according to the following processes. PhNH<sub>2</sub> 3.5 refluxed with meso-(MeO<sub>2</sub>CCHBrCH<sub>2</sub>)<sub>2</sub> 1 mole gives 68% di-Me 1-phenyl-2,5-pyrrolidinedicarboxylate, b<sub>27</sub> 220-30°, m. 88°. A solution of BuNH<sub>2</sub> 3 and meso-(EtO<sub>2</sub>CCHBrCH<sub>2</sub>)<sub>2</sub> (I) 1 mole in C<sub>6</sub>H<sub>6</sub> allowed to heat spontaneously, refluxed to complete the reaction, treated with a little Et<sub>2</sub>O, freed of salt, extracted with 6 N H<sub>2</sub>SO<sub>4</sub>, the extract

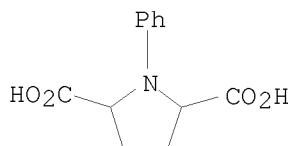
neutralized with Na<sub>2</sub>CO<sub>3</sub>, and the oil taken up in Et<sub>2</sub>O and distilled give 60% 1-butyl-2,5-dicarbethoxypyrrolidine, b<sub>1-2</sub> 155-6°, n<sub>D20</sub> 1.4514. PhNH<sub>2</sub> 327, I 360, and KI 5 parts are warmed gently to initiate a violent reaction, then heated at 85-90°, the product suspended in 6 N HCl, extracted with Et<sub>2</sub>O, and the exts. washed, dried, filtered, and distilled to give

90% di-Et 1-phenyl-2,5-pyrrolidinedicarboxylate, b<sub>0.5</sub> 144°, n<sub>D21.5</sub> 1.5230. 1 30, cyclohexylamine (II) 25, pulverized KI 1, and C<sub>6</sub>H<sub>6</sub> 75 parts let stand several hrs., refluxed, cooled, the mixture filtered, extracted with 70 cc. of 6 N H<sub>2</sub>SO<sub>4</sub>, the extract neutralized with Na<sub>2</sub>CO<sub>3</sub>, and the oil taken up in Et<sub>2</sub>O and distilled give 85.5% 1-cyclohexyl-2,5-dicarbethoxypyrrolidine (III), b<sub>1</sub> 133°, n<sub>D20</sub> 1.4738. 0Similarly, I 1, II 1, pulverized K<sub>2</sub>CO<sub>3</sub> 1 mole, and a little KI in 9 hrs. give 50% III; extending the reaction time to 52 hrs. gives 54% III. Other 1-substituted-2,5-dicarbethoxypyrrolidines prepared are: Me, b<sub>23</sub> 158-63°, n<sub>D20</sub> 1.4595; Et, b<sub>3-4</sub> 119-21°, n<sub>D20</sub> 1.4530; Pr, b<sub>5</sub> 130-1°, n<sub>D20</sub> 1.4503; iso-Bu, b<sub>1-1.5</sub> 115-16°, n<sub>D20</sub> 1.4498; hexyl, b<sub>1</sub> 117°, n<sub>D20</sub> 1.4529; benzyl, b<sub>1</sub> 138°, n<sub>D20</sub> 1.5042; 2-methoxyethyl, b<sub>1</sub> 108-9°, n<sub>D20</sub> 1.4550; phenethyl, b<sub>1</sub> 154-5°, n<sub>D20</sub> 1.5026; 2-acetamidoethyl, b<sub>1</sub> 168°, n<sub>D20</sub> 1.4657; Ph(alkyl-methyl)(?), m. 88°; o-tolyl, b<sub>0.5</sub> 129-30°, n<sub>D20</sub> 1.5108; m-tolyl, b<sub>0.5</sub> 136-7°, n<sub>D21.5</sub> 1.5215; p-tolyl, b<sub>0.5</sub> 164-5°, n<sub>D21.5</sub> 1.5226; p-C<sub>1</sub>C<sub>6</sub>H<sub>4</sub> b<sub>0.5</sub> 158°, n<sub>D21.5</sub> 1.5342; 2,4-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, b<sub>0.5</sub> 135-6°, n<sub>D21.5</sub> 1.5081; 3,5-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, b<sub>0.5</sub> 145-6°, n<sub>D21.5</sub> 1.5170; p-Ac-NHC<sub>6</sub>H<sub>5</sub>, decomposition 136°, n<sub>D21.5</sub> 1.5417; p-AcC<sub>6</sub>H<sub>4</sub>, decompose 136°, n<sub>D21.5</sub> 1.5459. Na 1 in Et<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>OH (IV) 250 and the product

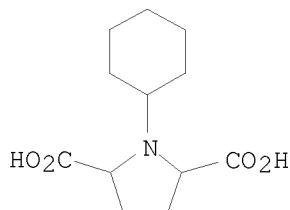
heated at 160-70° with 1-methyl-2,5-dicarbethoxypyrrolidine 53 parts gives 41% bis(2-diethyl-aminoethyl) 1-methyl-2,5-pyrrolidinedicarboxylate (V), b1 172-81°, nD20 1.4690. Similarly prepared are the 1-Et analog of V, b1 168.5-9° nD20 1.4678 (HCl salt, too hygroscopic to determine the m.p.); bis(3-diethylaminopropyl) 1-butyl-2,5-pyrrolidinedicarboxylate (VI), b1 186°, nD20 1.4619; 60% of the 1-cyclohexyl analog of VI, b1 203-4°, nD20 1.4803; bis[2-(4-morpholinyl)ethyl] 1-butyl-2,5-pyrrolidinedicarboxylate; and the 1-benzyl analog of V, b0.5 196-8°, nD20 1.4985. Na 1.5 dissolved in IV 540 and the product heated at 165° with 1-phenyl-2,5-dicarbethoxypyrrolidine 100 parts gives the 1-Ph analog of V, b0.5 189-91°, nD21.5 1.5121. Similarly prepared are the following analogs of V: p-tolyl, b0.5 175-8°, nD21.5 1.5144; 2,4-Me2C6H3, b1 187-90°, nD21.5 1.5023; Pr, b0.2 154-5°, nD20 1.4660; Bu, b1 169-70°, nD20 1.4664; iso-Bu, b1 155-6°, nD20 1.4656; hexyl, b1 179-80°, nD20 1.4668; cyclohexyl, b1 198°, nD20 1.4820; MeOCH2CH2, b1 175-7°, nD20 1.4695; PhCH2CH2, b1 206°, nD20 1.5002; o-tolyl, b0.5 180°, nD21.5 1.5035; m-tolyl, b0.5 195-6°, nD21.5 1.5113; p-ClC6H4, b1 207-8°, nD21.5 1.5203; and 2,5-Me2C6H3, b0.5 198-200°, nD21.5 1.5092. The compds. prepared are useful as local anesthetics and antispasmodics.

IT 859957-82-7, 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl-  
 860360-08-3, 2,5-Pyrrolidinedicarboxylic acid, 1-cyclohexyl-  
 860360-10-7, 2,5-Pyrrolidinedicarboxylic acid, 1-(p-chlorophenyl)-  
 860360-52-7, 2,5-Pyrrolidinedicarboxylic acid, 1-(2,4-xylyl)-  
 860360-54-9, 2,5-Pyrrolidinedicarboxylic acid, 1-p-tolyl-  
 860360-56-1, 2,5-Pyrrolidinedicarboxylic acid, 1-o-tolyl-  
 860360-58-3, 2,5-Pyrrolidinedicarboxylic acid, 1-m-tolyl-  
 (esters)

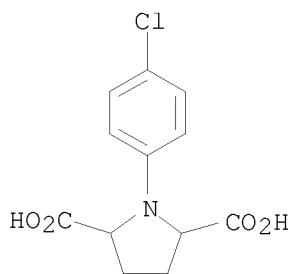
RN 859957-82-7 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl- (CA INDEX NAME)



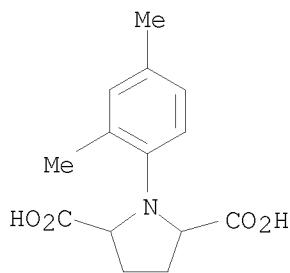
RN 860360-08-3 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 1-cyclohexyl- (CA INDEX NAME)



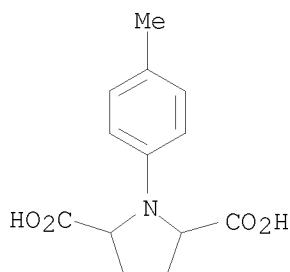
RN 860360-10-7 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-chlorophenyl)- (CA INDEX NAME)



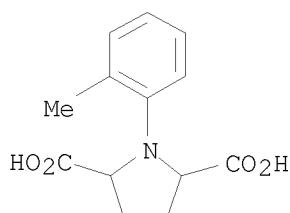
RN 860360-52-7 CAPLUS  
CN 2,5-Pyrrolidinedicarboxylic acid, 1-(2,4-dimethylphenyl)- (CA INDEX NAME)



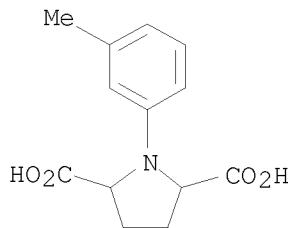
RN 860360-54-9 CAPLUS  
CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-methylphenyl)- (CA INDEX NAME)



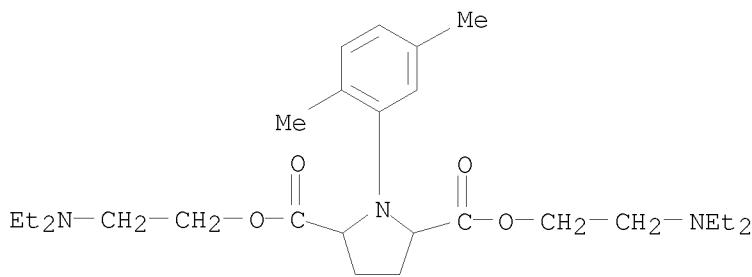
RN 860360-56-1 CAPLUS  
CN 2,5-Pyrrolidinedicarboxylic acid, 1-(2-methylphenyl)- (CA INDEX NAME)



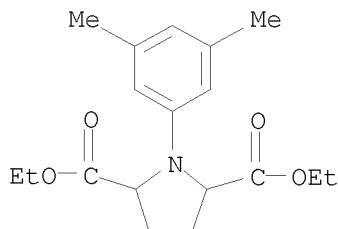
RN 860360-58-3 CAPLUS  
CN 2,5-Pyrrolidinedicarboxylic acid, 1-(3-methylphenyl)- (CA INDEX NAME)



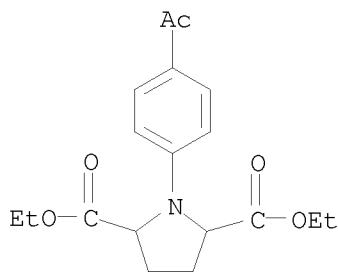
IT 857760-50-0P, 2,5-Pyrrolidinedicarboxylic acid, 1-(2,5-xylyl)-,  
 bis(2-diethylaminoethyl) ester 857760-52-2P,  
 2,5-Pyrrolidinedicarboxylic acid, 1-(3,5-xylyl)-, diethyl ester  
 860360-12-9P, 2,5-Pyrrolidinedicarboxylic acid,  
 1-(p-acetylphenyl)-, diethyl ester 860360-14-1P,  
 2,5-Pyrrolidinedicarboxylic acid, 1-(p-acetamidophenyl)-, diethyl ester  
 RL: PREP (Preparation)  
 (preparation of)  
 RN 857760-50-0 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 1-(2,5-dimethylphenyl)-,  
 2,5-bis[2-(diethylamino)ethyl] ester (CA INDEX NAME)



RN 857760-52-2 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 1-(3,5-dimethylphenyl)-, 2,5-diethyl  
 ester (CA INDEX NAME)

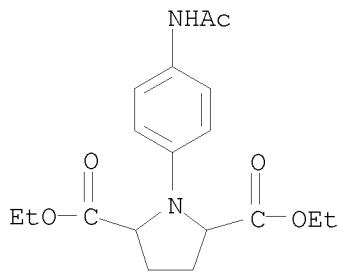


RN 860360-12-9 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-acetylphenyl)-, 2,5-diethyl ester  
 (CA INDEX NAME)



RN 860360-14-1 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-(acetylamino)phenyl]-, 2,5-diethyl ester (CA INDEX NAME)



L3 ANSWER 60 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1949:46441 CAPLUS

DOCUMENT NUMBER: 43:46441

ORIGINAL REFERENCE NO.: 43:8380b-f

TITLE: Ring closure of N-alkoxalyl- $\beta$ -anilinopropionic acids

AUTHOR(S): Southwick, Philip L.; Seivard, Louis L.

SOURCE: Journal of the American Chemical Society (1949), 71, 2532-8

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 43:46441

AB KO<sub>2</sub>CCO<sub>2</sub>Me and SOC<sub>12</sub> (1 mol. each) give 63% MeO<sub>2</sub>CCOCl (I); EtO<sub>2</sub>CCOCl (II) results in 59% yield. PhNH<sub>2</sub> (3 mols.) in 75 ml. AcOH, treated (1 hr.) with 3 mols. CH<sub>2</sub>:CHCO<sub>2</sub>Me, gives 57% PhNHCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me; KOH in MeOH gives 65% of the acid (III). PhNHCHPhCH<sub>2</sub>CO<sub>2</sub>H and twice its weight of I, heated 0.5 hr. on the steam bath, give 85% N-methoxalyl- $\beta$ -anilino- $\beta$ -phenylpropionic acid (IV), m. 127-8° (m.ps. corrected) (Me ester, m. 75-7°, 83%); N-ethoxalyl homolog (V), m. 111-13°, 78%; N-Ethoxalyl- $\beta$ -anilinopropionic acid (VI), m. 91-2°, 58%; N-ethoxalyl- $\beta$ -amino- $\beta$ -phenylpropionic acid (VII), m. 116-18°, 43%. IV and an equal weight of I or II in 2 ml. CHCl<sub>3</sub> per g. IV (dioxane can be used as the solvent), treated with C<sub>5</sub>H<sub>5</sub>N equal to the weight of the acid, kept 30 min. at room temperature, diluted with 5 vols.

CHCl<sub>3</sub>,

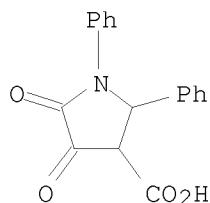
shaken 2 hrs. with an equal volume of H<sub>2</sub>O, and the CHCl<sub>3</sub> layer extracted with excess 5% NaHCO<sub>3</sub> and precipitated with 5% HCl, give 26% 1,5-diphenyl-2-keto-3-methoxy-3-pyrrolidine-4-carboxylic acid (VIII), m. 196-8°; Me ester, m. 128.5-30°; Et ester, m. 83-5°. V yields 32% of the 3-EtO analog (IX), m. 214-15°; Me ester (X), m. 91-2°; 3 g. V in 7

cc. Ac<sub>2</sub>O and 7 g. C<sub>5</sub>H<sub>5</sub>N, heated 3 hrs. on the steam bath, gives 10% IX; no reaction occurs with Ac<sub>2</sub>O or C<sub>5</sub>H<sub>5</sub>N alone. VI yields 15% 1-phenyl-2-keto-3-ethoxy-Δ<sub>3</sub>-pyrroline-4-carboxylic acid (XI), m. 189-91°; Me ester (XII), m. 75.5-7°. III and II in the presence of C<sub>5</sub>H<sub>5</sub>N give XI; in the absence of C<sub>5</sub>H<sub>5</sub>N, the product is VI. PhCH<sub>2</sub>NPh and MeO<sub>2</sub>CCOCH<sub>2</sub>CO<sub>2</sub>Et give 66% Me 1,5-diphenyl-2,3-pyrrolidinedione-4-carboxylate (XIII), m. 201-3°; MeCHN<sub>2</sub> gives the Et ester. PhNHCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me (7.2 g.) and 4.8 g. (CO<sub>2</sub>Me)<sub>2</sub> in 50 ml. ether, treated (15 min.) with 2.5 g. MeONa in 50 ml. ether and refluxed 2 hrs., give 38% Me 1-phenyl-2,3-pyrrolidinedione-4-carboxylate, m. 185-7°; MeCHN<sub>2</sub> gives XII. The Et ester corresponding to XIII and CH<sub>2</sub>N<sub>2</sub> give the Et ester of VIII. A mechanism is proposed for the ring closure reaction which relates it to the Perkin reaction and to the Claisen condensation.

IT 873399-08-7, 3-Pyrrolidinedicarboxylic acid, 4,5-dioxo-1,2-diphenyl- (esters)

RN 873399-08-7 CAPLUS

CN 3-Pyrrolidinedicarboxylic acid, 4,5-dioxo-1,2-diphenyl- (CA INDEX NAME)



L3 ANSWER 61 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1947:1129 CAPLUS

DOCUMENT NUMBER: 41:1129

ORIGINAL REFERENCE NO.: 41:213h-i,214a

TITLE: Pharmacological activity of basic alkyl esters of substituted pyrrolidine dicarboxylic acids. II. Action on intestine, uterus, and blood pressure

Loomis, Ted. A.; Schaffer, Norwood K.

AUTHOR(S):

CORPORATE SOURCE: Yale Univ.

SOURCE: Yale Journal of Biology and Medicine (1946), 18, 171-84

CODEN: YJBMAU; ISSN: 0044-0086

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Fourteen of these compds. II, III, IV, V, VI, VII, VIII, X, XI, XII, XIII, XIV, XV, and XVI produced a spasmotic response in the circular muscle of the intact duodenum of the cat. The response of 15 mg./kg. of the most active was equivalent to 2 mg./kg. of BaCl<sub>2</sub>. I, II, III, IV, V, VI, VIII, IX, XIV, XV, and XVI produced a spasmotic response in the intact uterus of the cat. All compds. caused fall in arterial blood pressure. VII, IX, XI, XII, XIII, and XVI were very toxic, 10 mg./kg. causing a 100% fall in blood pressure and heart rate.

IT 859957-82-7P, 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl-, bis(2-diethylaminoethyl) and bis(3-diethylaminopropyl) esters  
 860360-52-7P, 2,5-Pyrrolidinedicarboxylic acid, 1-[2,4-xylyl]-, bis(2-diethylaminoethyl) esters 860360-56-1P,  
 2,5-Pyrrolidinedicarboxylic acid, 1-o-tolyl-, bis(2-diethylaminoethyl) esters 860360-58-3P, 2,5-Pyrrolidinedicarboxylic acid,  
 1-m-tolyl-, bis(2-diethylaminoethyl) esters 874496-93-2P,  
 2,5-Pyrrolidinedicarboxylic acid, 1-p-tolyl-, 2-diethylaminoethyl ethyl ester 874496-98-7P, 2,5-Pyrrolidinedicarboxylic acid,  
 1-(p-chlorophenyl)-, bis(2-diethylaminoethyl) ester 875233-90-2P  
 , 2,5-Pyrrolidinedicarboxylic acid, 1-cyclohexyl-, bis(3-

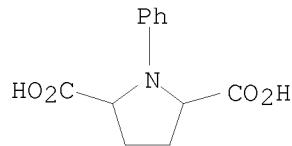
diethylaminopropyl) ester

RL: PREP (Preparation)

(preparation of)

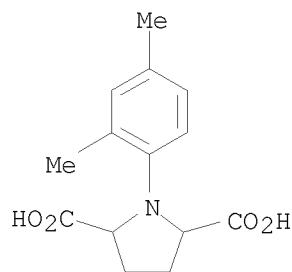
RN 859957-82-7 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl- (CA INDEX NAME)



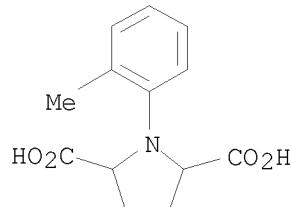
RN 860360-52-7 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-(2,4-dimethylphenyl)- (CA INDEX NAME)



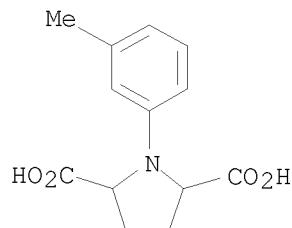
RN 860360-56-1 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-(2-methylphenyl)- (CA INDEX NAME)



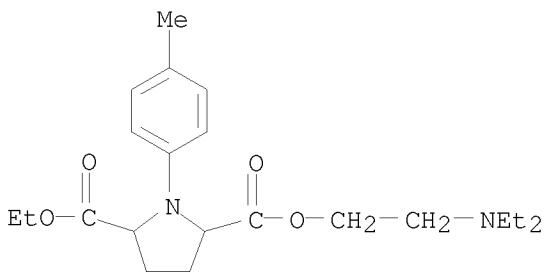
RN 860360-58-3 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-(3-methylphenyl)- (CA INDEX NAME)

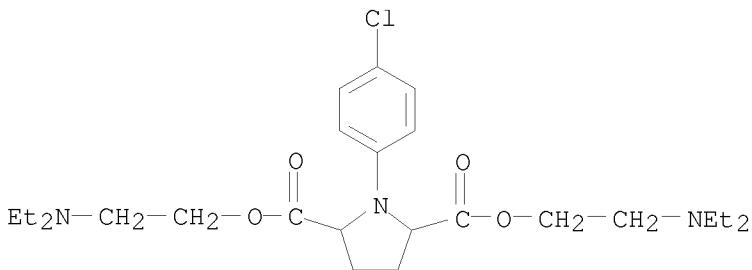


RN 874496-93-2 CAPLUS

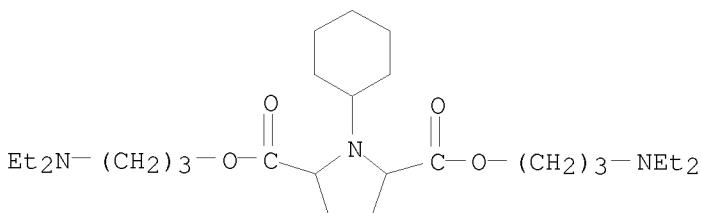
CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-methylphenyl)-,  
2-[2-(diethylamino)ethyl] 5-ethyl ester (CA INDEX NAME)



RN 874496-98-7 CAPLUS  
CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-chlorophenyl)-,  
2,5-bis[2-(diethylamino)ethyl] ester (CA INDEX NAME)



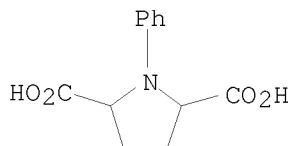
RN 875233-90-2 CAPLUS  
CN 2,5-Pyrrolidinedicarboxylic acid, 1-cyclohexyl-, 2,5-bis[3-(diethylamino)propyl] ester (CA INDEX NAME)



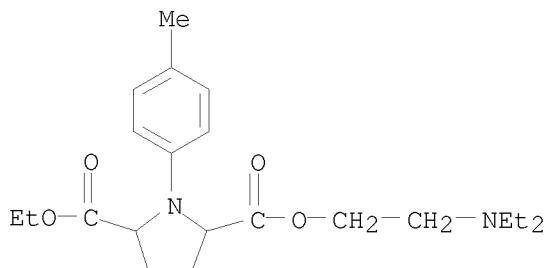
L3 ANSWER 62 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1947:1128 CAPLUS  
DOCUMENT NUMBER: 41:1128  
ORIGINAL REFERENCE NO.: 41:213f-h  
TITLE: Pharmacological activity of basic alkyl esters of substituted pyrrolidine dicarboxylic acids. I. Local anesthetic activity and toxicity  
AUTHOR(S): Schaffer, Norwood K.; Loomis, Ted A.  
CORPORATE SOURCE: Yale Univ.  
SOURCE: Yale Journal of Biology and Medicine (1946), 18, 157-64  
DOCUMENT TYPE: CODEN: YJBMAU; ISSN: 0044-0086  
LANGUAGE: Journal  
GI For diagram(s), see printed CA Issue.  
AB The local-anesthetic activity and toxicity were measured on the rabbit

cornea and by intraperitoneal injection in mice for 16 derivs. of 2,5-pyrrolidinedicarboxylic acid, (NR.CH(COOCH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub>).CH<sub>2</sub>.CH<sub>2</sub>.CHCOOCH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub>) where R = Et (I), MeOCH<sub>2</sub>CH<sub>2</sub> (II), iso-Bu (III), hexyl (IV), benzyl (V), Ph (VI), o-tolyl (VII), m-tolyl (VIII), phenethyl (IX), p-C<sub>1</sub>C<sub>6</sub>H<sub>4</sub> (X), 2,4-xylyl (XI), and 3,5-xylyl (XII); (NR.CH(COOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub>).CH<sub>2</sub>.CH<sub>2</sub>.CHCOOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub>) where R = Ph (XIII), cyclohexyl (XIV), and Bu (XV), and p-MeC<sub>6</sub>H<sub>4</sub>N.CH(COOEt).CH<sub>2</sub>.CH<sub>2</sub>.CHCOOCH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub> (XVI). IV and V had the highest therapeutic indexes (3.4 times that of cocaine); VII, VIII, IX, XI, XII, and XVI had therapeutic indexes greater than cocaine. These were less toxic than cocaine.

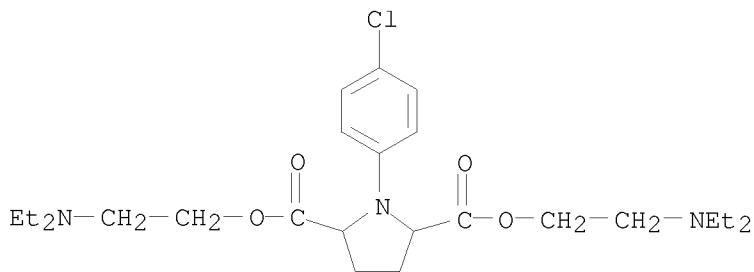
IT 859957-82-7P, 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl-  
 874496-93-2P, 2,5-Pyrrolidinedicarboxylic acid, 1-p-tolyl-,  
 2-diethylaminoethyl ethyl ester 874496-98-7P,  
 2,5-Pyrrolidinedicarboxylic acid, 1-(p-chlorophenyl)-,  
 bis(2-diethylaminoethyl) ester 875233-90-2P,  
 2,5-Pyrrolidinedicarboxylic acid, 1-cyclohexyl-, bis(3-diethylaminopropyl)  
 ester  
 RL: PREP (Preparation)  
 (preparation of)  
 RN 859957-82-7 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl- (CA INDEX NAME)



RN 874496-93-2 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-methylphenyl)-,  
 2-[2-(diethylamino)ethyl] 5-ethyl ester (CA INDEX NAME)

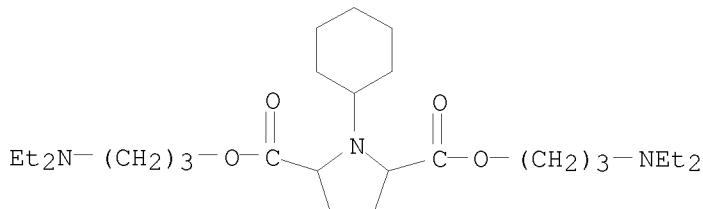


RN 874496-98-7 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-chlorophenyl)-,  
 2,5-bis[2-(diethylamino)ethyl] ester (CA INDEX NAME)



RN 875233-90-2 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-cyclohexyl-, 2,5-bis[3-(diethylamino)propyl] ester (CA INDEX NAME)



L3 ANSWER 63 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1946:27690 CAPLUS

DOCUMENT NUMBER: 40:27690

ORIGINAL REFERENCE NO.: 40:5427c-i, 5428a-b

TITLE: Condensation products of  $\alpha, \gamma$ -diketo acids and their esters

AUTHOR(S): Keskin, Halit

CORPORATE SOURCE: Chemical Inst. II, Univ. of Istanbul, Turk.

SOURCE: Rev. faculte sci. univ. Istanbul (1946), 11A(No. 1/2), 1-23

DOCUMENT TYPE: Journal

LANGUAGE: French

GI For diagram(s), see printed CA Issue.

AB cf. C.A. 40, 1490.4, 9 18226. To 1 g. enanthylpyruvic acid in 5 ml. EtOH was added a solution of 0.35 g. H2NNH2.HCl, and then 1 g. Na2CO3. The next day the solution was acidified with H2SO4 and extracted with Et2O. The extract was

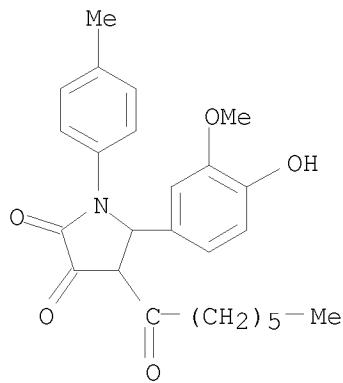
dried over Na2SO4 and evaporated on a watch glass, yielding 0.9 g. of 5-hexylisoxazole-3-carboxylic acid (I). Recrystd. from H2O or petr. ether, the white product m. 104-5°. The 5-octyl derivative, prepared similarly from nonanoylpyruvic acid, m. 101-2°. Neither of the condensation products in alc. gives a color reaction with FeCl3. Both are monobasic, as shown by titration with NaOH. The Et esters of  $\alpha, \gamma$ -diketo acids, condensed simultaneously with aromatic amines, RNH2, and aldehydes, R'CHO, yield 4,5-diketopyrrolidines consisting of an equilibrium mixture of the keto (II) and enol (III) forms.

The

enolization does not take place in the ring, as suggested by Schiff and Gigli (Ber. 31, 1307(1898)), but in the side chain. 1-p-Tolyl-2-phenyl-3-propionyl-4,5-diketopyrrolidine has been prepared by adding 0.9 ml. EtCOCH2COCO2Et and 0.5 ml. of BzH to 0.5 g. p-toluidine in 5 ml. of C6H6. After 2 days, the crystals were collected and washed with a little EtOH, yielding 1.3 g. Recrystd. from EtOH, the white crystals m. 222-4°.

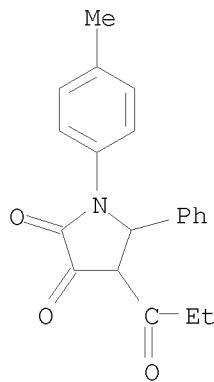
The following derivs. of 4,5-diketopyrrolidine were made similarly:  
1-phenyl-2-(p-methoxyphenyl)-3-butyryl, white crystals, m. 206-7°;  
1-p-tolyl-2-(p-methoxyphenyl)-3-butyryl, white crystals, m. 189-90°; 1-phenyl-2-(p-methoxyphenyl)-3-isovaleryl, m. 216-17°; 1-p-tolyl-2-(p-methoxyphenyl)-3-isovaleryl, m. 200-1°; 1-phenyl-2-(p-methoxyphenyl)-3-caproyl, white crystals, m. 182°; 1-p-tolyl-2-(p-methoxyphenyl)-3-caproyl, white crystals, m. 190-1°; 1,2-diphenyl-3-enanthyl, m. 182°;  
1-p-tolyl-2-phenyl-3-enanthyl, white crystals, m. 186°;  
1-phenyl-2-(p-methoxyphenyl)-3-enanthyl, m. 173°;  
1-p-tolyl-2-(p-methoxyphenyl)-3-enanthyl, m. 206-7°;  
1-phenyl-2-(p-dimethylaminophenyl)-3-enanthyl, pale yellow, m. 180-1°; 1-p-tolyl-2-(p-dimethylaminophenyl)-3-enanthyl, pale yellow, m. 232°; 1-phenyl-2-(4-hydroxy-3-methoxyphenyl)-3-enanthyl, white crystals, m. 204°; 1-p-tolyl-2-(4-hydroxy-3-methoxyphenyl)-3-enanthyl, m. 208°; 1-(1-naphthyl)-2-phenyl-3-enanthyl, m. 194-5°; 1-(2-naphthyl)-2-phenyl-3-enanthyl, m. 192°;  
1,2-diphenyl-3-nonanoyl, m. 173°; 1-p-tolyl-2-phenyl-3-nonanoyl m. 184°; 1-phenyl-2-(p-methoxyphenyl)-3-nonanoyl, m. 139°;  
1-p-tolyl-2-(p-methoxyphenyl)-3-nonanoyl, m. 171-2°;  
1-phenyl-2-(p-dimethylaminophenyl)-3-nonanoyl, pale yellow crystals, m. 182-3°; 1-p-tolyl-2-(p-dimethylaminophenyl)-3-nonanoyl, yellow crystals, m. 189°; 1-m-tolyl-2-(4-hydroxy-3-methoxyphenyl)-3-nonanoyl, m. 168-9°; 1-(1-naphthyl)-2-phenyl-3-nonanoyl; white crystals, m. 175-6°; 1-(2-naphthyl)-2-phenyl-3-nonanoyl, white crystals, m. 182-3°; 1-phenyl-2-(p-methoxyphenyl)-3-decanoyl, m. 140-1°; 1-p-tolyl-2-(p-methoxyphenyl)-3-decanoyl, m. 149-50°; 1-phenyl-2-(p-methoxyphenyl)-3-dodecanoyl, m. 115-17°; 1-p-tolyl-2-(p-methoxyphenyl)-3-dodecanoyl, m. 142°. All these substituted diketopyrrolidines have 1 acid function, and give a blood-red color reaction with FeCl<sub>3</sub> in EtOH.

IT 854896-66-5P, 2,3-Pyrrolidinedione, 4-enanthyl-5-(4-hydroxy-3-methoxyphenyl)-1-p-tolyl- 858273-78-6P, 2,3-Pyrrolidinedione, 5-phenyl-4-propionyl-1-p-tolyl- 858274-03-0P, 2,3-Pyrrolidinedione, 4-lauroyl-5-(p-methoxyphenyl)-1-p-tolyl- 858274-04-1P, 2,3-Pyrrolidinedione, 4-lauroyl-5-(p-methoxyphenyl)-1-phenyl- 858274-22-3P, 2,3-Pyrrolidinedione, 4-caproyl-5-(p-methoxyphenyl)-1-p-tolyl- 858274-23-4P, 2,3-Pyrrolidinedione, 4-caproyl-5-(p-methoxyphenyl)-1-phenyl- 858274-24-5P, 2,3-Pyrrolidinedione, 4-butryryl-5-(p-methoxyphenyl)-1-p-tolyl- 858274-25-6P, 2,3-Pyrrolidinedione, 4-butryryl-5-(p-methoxyphenyl)-1-phenyl- 861035-28-1P, 2,3-Pyrrolidinedione, 4-isovaleryl-5-(p-methoxyphenyl)-1-p-tolyl- 861035-30-5P, 2,3-Pyrrolidinedione, 4-isovaleryl-5-(p-methoxyphenyl)-1-phenyl- 861035-37-2P, 2,3-Pyrrolidinedione, 4-enanthyl-5-phenyl-1-p-tolyl- 861035-39-4P, 2,3-Pyrrolidinedione, 4-enanthyl-1-[2-naphthyl]-5-phenyl- 861035-41-8P, 2,3-Pyrrolidinedione, 4-enanthyl-1-[1-naphthyl]-5-phenyl- 861035-43-0P, 2,3-Pyrrolidinedione, 4-enanthyl-5-(p-methoxyphenyl)-1-p-tolyl- 861035-45-2P, 2,3-Pyrrolidinedione, 4-enanthyl-5-(p-methoxyphenyl)-1-phenyl- 861035-47-4P, 2,3-Pyrrolidinedione, 4-enanthyl-5-(4-hydroxy-2-methoxyphenyl)-1-phenyl- 861035-49-6P, 2,3-Pyrrolidinedione, 4-enanthyl-1,5-diphenyl- 861035-59-8P, 2,3-Pyrrolidinedione, 5-(p-dimethylaminophenyl)-4-enanthyl-1-p-tolyl- 861035-61-2P, 2,3-Pyrrolidinedione, 5-(p-dimethylaminophenyl)-4-enanthyl-1-phenyl-  
RL: PREP (Preparation)  
(preparation of)  
RN 854896-66-5 CAPLUS  
CN 2,3-Pyrrolidinedione, 5-(4-hydroxy-3-methoxyphenyl)-1-(4-methylphenyl)-4-(1-oxoheptyl)- (CA INDEX NAME)



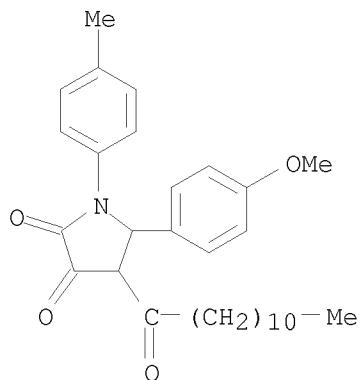
RN 858273-78-6 CAPLUS

CN 2,3-Pyrrolidinedione, 1-(4-methylphenyl)-4-(1-oxopropyl)-5-phenyl- (CA INDEX NAME)



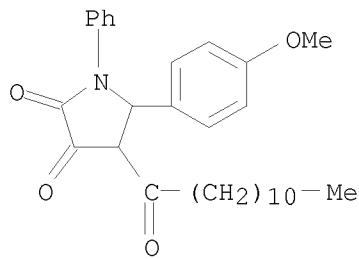
RN 858274-03-0 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-1-(4-methylphenyl)-4-(1-oxododecyl)- (CA INDEX NAME)



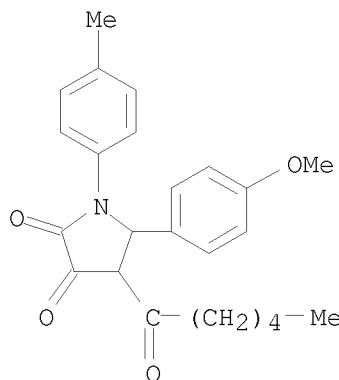
RN 858274-04-1 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-4-(1-oxododecyl)-1-phenyl- (CA INDEX NAME)



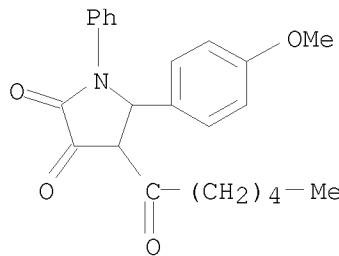
RN 858274-22-3 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-1-(4-methylphenyl)-4-(1-oxohexyl)- (CA INDEX NAME)



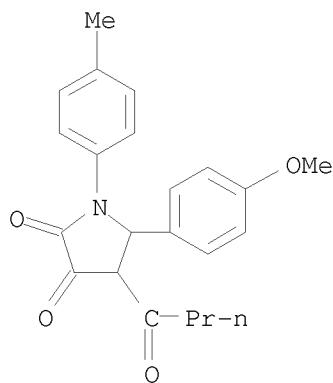
RN 858274-23-4 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-4-(1-oxohexyl)-1-phenyl- (CA INDEX NAME)



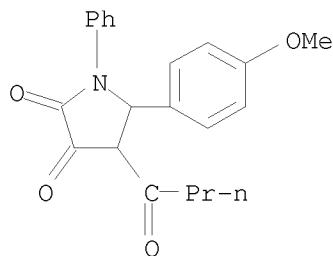
RN 858274-24-5 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-1-(4-methylphenyl)-4-(1-oxobutyl)- (CA INDEX NAME)



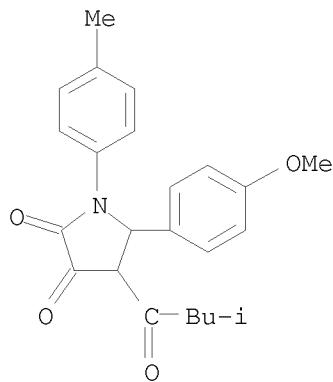
RN 858274-25-6 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-4-(1-oxobutyl)-1-phenyl- (CA INDEX NAME)



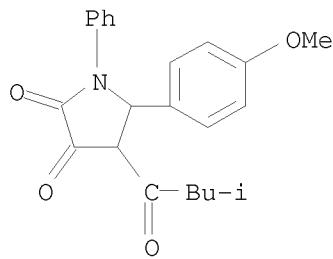
RN 861035-28-1 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-4-(3-methyl-1-oxobutyl)-1-(4-methylphenyl)- (CA INDEX NAME)



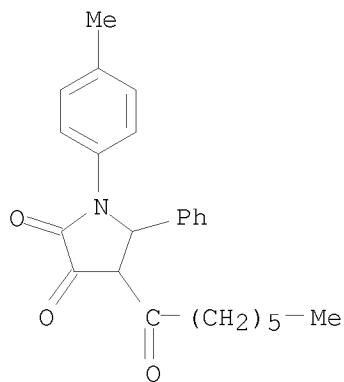
RN 861035-30-5 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-4-(3-methyl-1-oxobutyl)-1-phenyl- (CA INDEX NAME)



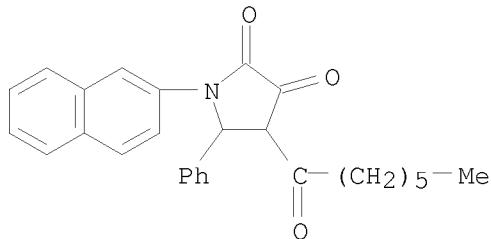
RN 861035-37-2 CAPLUS

CN 2,3-Pyrrolidinedione, 1-(4-methylphenyl)-4-(1-oxoheptyl)-5-phenyl- (CA INDEX NAME)



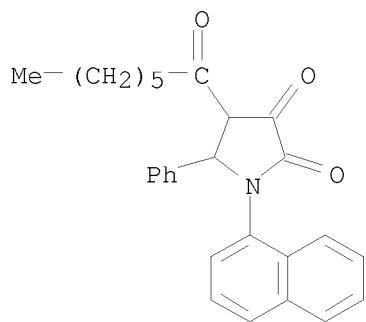
RN 861035-39-4 CAPLUS

CN 2,3-Pyrrolidinedione, 1-(2-naphthalenyl)-4-(1-oxoheptyl)-5-phenyl- (CA INDEX NAME)



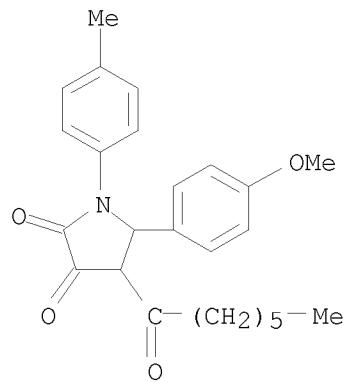
RN 861035-41-8 CAPLUS

CN 2,3-Pyrrolidinedione, 1-(1-naphthalenyl)-4-(1-oxoheptyl)-5-phenyl- (CA INDEX NAME)



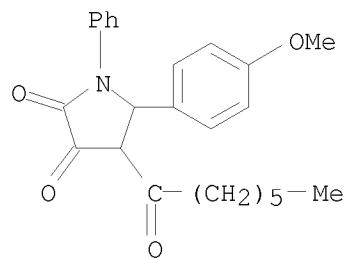
RN 861035-43-0 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-1-(4-methylphenyl)-4-(1-oxoheptyl)- (CA INDEX NAME)



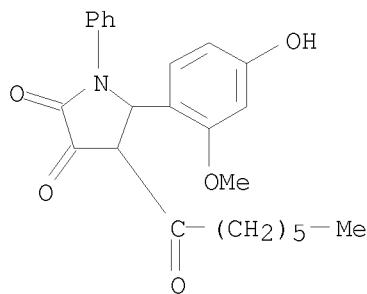
RN 861035-45-2 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-methoxyphenyl)-4-(1-oxoheptyl)-1-phenyl- (CA INDEX NAME)



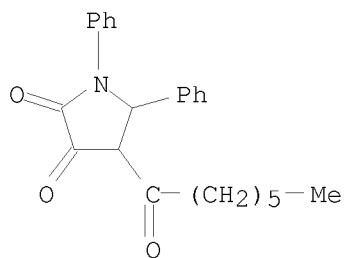
RN 861035-47-4 CAPLUS

CN 2,3-Pyrrolidinedione, 5-(4-hydroxy-2-methoxyphenyl)-4-(1-oxoheptyl)-1-phenyl- (CA INDEX NAME)



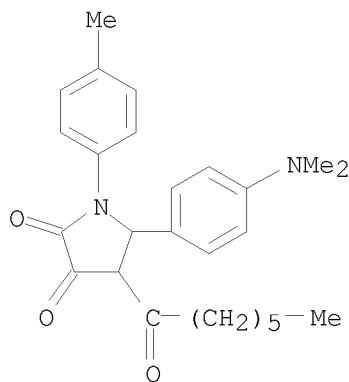
RN 861035-49-6 CAPLUS

CN 2,3-Pyrrolidinedione, 4-(1-oxoheptyl)-1,5-diphenyl- (CA INDEX NAME)



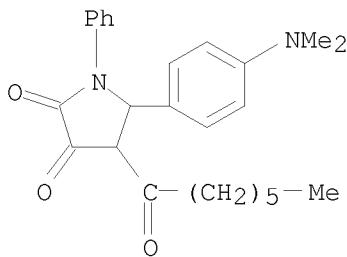
RN 861035-59-8 CAPLUS

CN 2,3-Pyrrolidinedione, 5-[4-(dimethylamino)phenyl]-1-(4-methylphenyl)-4-(1-oxoheptyl)- (CA INDEX NAME)



RN 861035-61-2 CAPLUS

CN 2,3-Pyrrolidinedione, 5-[4-(dimethylamino)phenyl]-4-(1-oxoheptyl)-1-phenyl- (CA INDEX NAME)



L3 ANSWER 64 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1939:55382 CAPLUS  
 DOCUMENT NUMBER: 33:55382  
 ORIGINAL REFERENCE NO.: 33:7963b-h  
 TITLE: Pyrrolidine derivatives  
 INVENTOR(S): Dohrn, Max; Nahme, Hans  
 PATENT ASSIGNEE(S): Schering A.-G.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Unavailable  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 678152		19390711	DE 1937-SC114287	19371119

AB Substitution products of 4,5-diketo-pyrrolidine (I) are obtained by condensing an easily saponifiable derivative of a hydroxybenzaldehyde, e. g., an acyloxybenzaldehyde or a hydroxybenzaldehyde alkyl-carbonic acid ester, with a primary aromatic, alicyclic or heterocyclic amine and an  $\alpha$ -keto carboxylic ester, e. g., an oxalacetic or acylpyruvic ester. The products may then be treated to remove the easily saponifiable group. In a typical example, p-OHCC6H4OCOOMe, PhNH<sub>2</sub> and AcCH<sub>2</sub>COOCOOEt are allowed to stand in benzene solution to yield 1-phenyl-3-acetyl-2-(4'-carbomethoxyoxyphenyl)-I, m. 205°, which yields 1-phenyl-3-acetyl-2-(4'-hydroxyphenyl)-I, m. 244-6°, when warmed with caustic alkali solution. Similarly, p-OHCC6H4OCOOMe, PhNH<sub>2</sub> and PhCOCH<sub>2</sub>COOCOOEt yield 1-phenyl-3-benzoyl-2-(4'-carbomethoxyoxyphenyl)-I, m. 238°, which yields 1-phenyl-3-benzoyl-2-(4'-hydroxyphenyl)-I, m. 248°, when saponified, and p-OHCC6H4OCOOMe, PhNH<sub>2</sub> and EtO-OCCOCH<sub>2</sub>COOCOOEt yield 1-phenyl-3-carbethoxy-2-(4'-carbomethoxyoxyphenyl)-I, m. 168-70°, which yields 1-phenyl-2-(4'-hydroxyphenyl)-I-3-carboxylic acid, decomposing 240°, when saponified. Examples are given also of the preparation of (a) 1-(4'-carbethoxyphenyl)-3-acetyl-2-(4'-carbomethoxyoxyphenyl)-I, m. 223°, which yields 1-(4'-carboxyphenyl)-3-acetyl-2-(4'-hydroxyphenyl)-I, m. 265°, when saponified, (b) 1-(4'-dimethylaminophenyl)-3-acetyl-2-(4'-carbomethoxyoxyphenyl)-I, m. 139-42°, and the corresponding 2-(4'-hydroxyphenyl) compound, m. 243°, (c) 1-(4'-iodophenyl)-3-acetyl-2-(4'-carbomethoxyoxyphenyl)-I, m. 225°, and the corresponding 2-(4'-hydroxyphenyl) compound, m. 255°, (d) 1-(3',4',5'-triodophenyl)-3-acetyl-2-(4'-carbomethoxyoxyphenyl)-I, m. 230° (decomposition), and the corresponding 2-(4'-hydroxyphenyl) compound, m. 263° (decomposition), (e) 1-(2'-butyloxy - 5' - pyridyl) - 3 - acetyl - 2 - (4' - carbomethoxyoxyphenyl)-I, m. 100°, and the corresponding 2-(4'-hydroxyphenyl) compound, m. 220°, (f) 1-(6'-quinolyl)-3-acetyl-2-(4'-carbomethoxyoxyphenyl)-I, decomposing above 270°, and the corresponding 2-(4'-hydroxyphenyl) compound, m. above 260° (decomposition), (g) 1-cyclohexyl-3-acetyl-2-(4'-carbomethoxyoxyphenyl)-I, m. 195-6°, and the corresponding

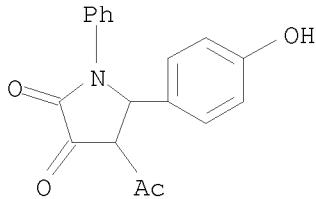
2-(4'-hydroxyphenyl) compound, m. 239°, (h) 1-phenyl-3-acetyl-2-(2'-carboethoxyoxyphenyl)-I, m. 171°, and the corresponding 2-(2'-hydroxyphenyl) compound, m. 198-200°, (i) 1-phenyl-3-acetyl-2-(3'-carbomethoxyoxyphenyl)-I, m. 191°, and the corresponding 2-(3'-hydroxyphenyl) compound, m. 183° (j) 1-phenyl-3-acetyl-2-(4'-acetoxyphenyl)-I, m. 205-6°, and the corresponding 2-(4'-hydroxyphenyl) compound, (k) 1-phenyl-3-acetyl-2-(4'-benzyloxyphenyl)-I, m. 236-7°. The products are useful as drugs or intermediates for drugs.

IT 852058-50-5, 2,3-Pyrrolidinedione, 4-acetyl-5-[p-hydroxyphenyl]-1-phenyl- 858274-45-0, 2,3-Pyrrolidinedione, 4-acetyl-5-[o-hydroxyphenyl]-1-phenyl- 858274-47-2, 2,3-Pyrrolidinedione, 4-acetyl-5-[m-hydroxyphenyl]-1-phenyl-

(and esters)

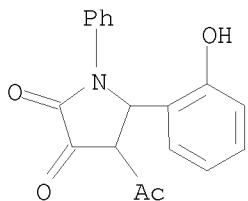
RN 852058-50-5 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(4-hydroxyphenyl)-1-phenyl- (CA INDEX NAME)



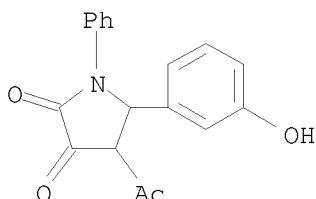
RN 858274-45-0 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(2-hydroxyphenyl)-1-phenyl- (CA INDEX NAME)



RN 858274-47-2 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(3-hydroxyphenyl)-1-phenyl- (CA INDEX NAME)

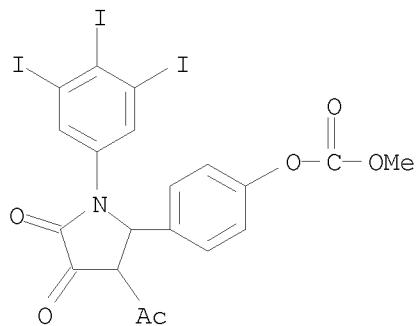


IT 858274-37-0P, 2,3-Pyrrolidinedione, 4-acetyl-5-(p-hydroxyphenyl)-1-(3,4,5-triiodophenyl)-, methyl carbonate 858274-39-2P, 2,3-Pyrrolidinedione, 4-acetyl-5-(p-hydroxyphenyl)-1-(3,4,5-triiodophenyl)- 858274-42-7P, 2,3-Pyrrolidinedione, 4-acetyl-5-(p-hydroxyphenyl)-1-(6-quinolyl)-, methyl carbonate 858274-43-8P, 2,3-Pyrrolidinedione, 4-acetyl-5-(p-hydroxyphenyl)-1-(6-quinolyl)-

858274-49-4P, 2,3-Pyrrolidinedione, 4-acetyl-5-(p-hydroxyphenyl)-1-(p-iodophenyl)-, methyl carbonate 861035-81-6P,  
 2,3-Pyrrolidinedione, 4-acetyl-5-(p-hydroxyphenyl)-1-(p-iodophenyl)-861035-84-9P, 2,3-Pyrrolidinedione, 4-acetyl-1-(p-dimethylaminophenyl)-5-(p-hydroxyphenyl)-, methyl carbonate 861035-85-0P, 2,3-Pyrrolidinedione, 4-acetyl-1-(p-dimethylaminophenyl)-5-(p-hydroxyphenyl)-861035-86-1P,  
 2,3-Pyrrolidinedione, 4-acetyl-1-cyclohexyl-5-(p-hydroxyphenyl)-, methyl carbonate 861035-87-2P, 2,3-Pyrrolidinedione,  
 4-acetyl-1-cyclohexyl-5-(p-hydroxyphenyl)-861035-88-3P,  
 2,3-Pyrrolidinedione, 4-acetyl-1-(p-carboxyphenyl)-5-(p-hydroxyphenyl)-, Et ester methyl carbonate 861035-89-4P, 2,3-Pyrrolidinedione,  
 4-acetyl-1-(p-carboxyphenyl)-5-(p-hydroxyphenyl)-861035-90-7P,  
 2,3-Pyrrolidinedione, 4-acetyl-1-(6-butoxy-3-pyridyl)-5-(p-hydroxyphenyl)-, methyl carbonate 861035-91-8P, 2,3-Pyrrolidinedione,  
 4-acetyl-1-(6-butoxy-3-pyridyl)-5-(p-hydroxyphenyl)-861035-92-9P,  
 2,3-Pyrrolidinedione, 4-acetyl-5-[p-(benzyloxy)phenyl]-1-phenyl-  
 RL: PREP (Preparation)  
 (preparation of)

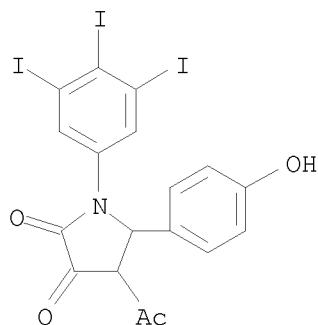
RN 858274-37-0 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(p-hydroxyphenyl)-1-(3,4,5-triiodophenyl)-, methyl carbonate (4CI) (CA INDEX NAME)



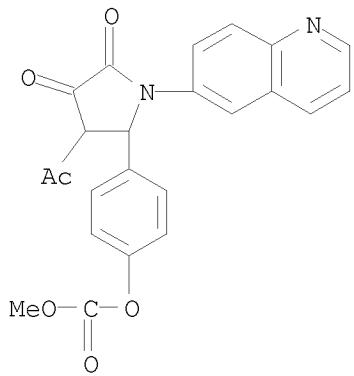
RN 858274-39-2 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(4-hydroxyphenyl)-1-(3,4,5-triiodophenyl)- (CA INDEX NAME)



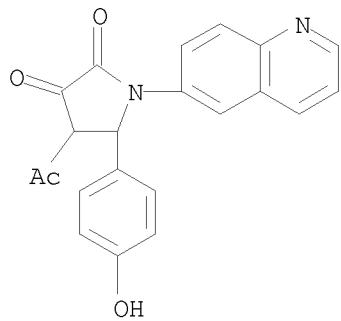
RN 858274-42-7 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(p-hydroxyphenyl)-1-(6-quinolyl)-, methyl carbonate (4CI) (CA INDEX NAME)



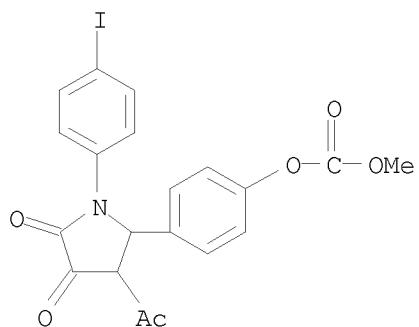
RN 858274-43-8 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(4-hydroxyphenyl)-1-(6-quinolinyl)- (CA INDEX NAME)



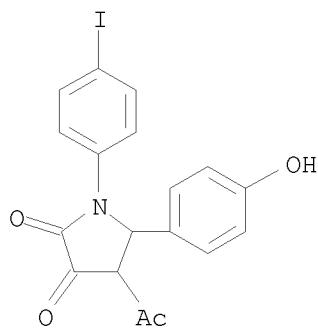
RN 858274-49-4 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(p-hydroxyphenyl)-1-(p-iodophenyl)-, methyl carbonate (4CI) (CA INDEX NAME)



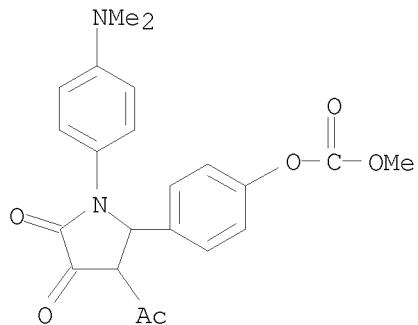
RN 861035-81-6 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(4-hydroxyphenyl)-1-(4-iodophenyl)- (CA INDEX NAME)



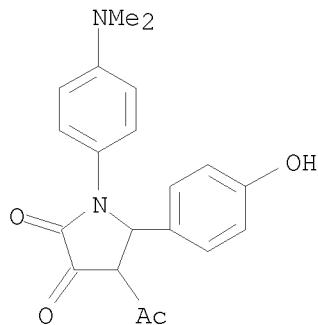
RN 861035-84-9 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-1-(p-dimethylaminophenyl)-5-(p-hydroxyphenyl)-, methyl carbonate (4CI) (CA INDEX NAME)



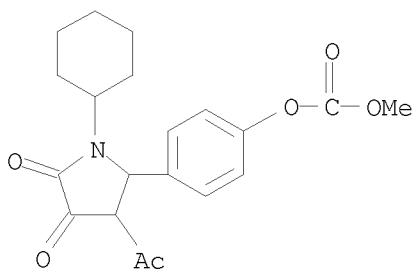
RN 861035-85-0 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-1-[4-(dimethylamino)phenyl]-5-(4-hydroxyphenyl)- (CA INDEX NAME)



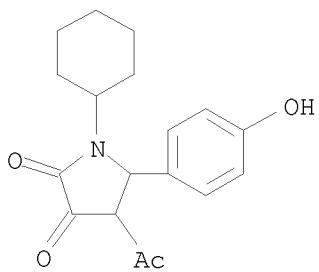
RN 861035-86-1 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-1-cyclohexyl-5-(p-hydroxyphenyl)-, methyl carbonate (4CI) (CA INDEX NAME)



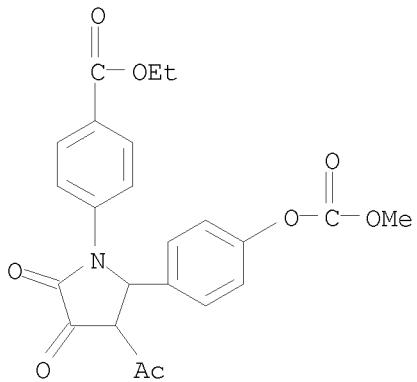
RN 861035-87-2 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-1-cyclohexyl-5-(4-hydroxyphenyl)- (CA INDEX NAME)



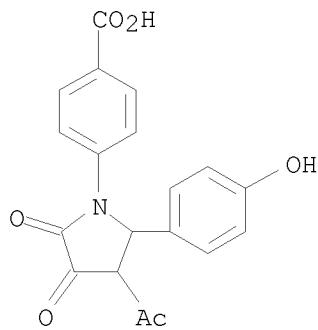
RN 861035-88-3 CAPLUS

CN INDEX NAME NOT YET ASSIGNED



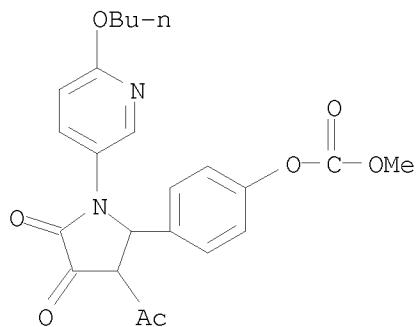
RN 861035-89-4 CAPLUS

CN INDEX NAME NOT YET ASSIGNED



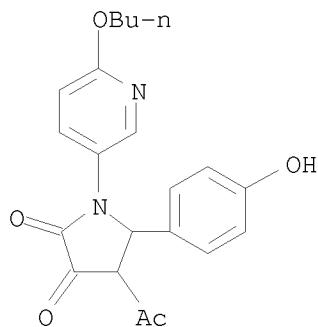
RN 861035-90-7 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-1-(6-butoxy-3-pyridyl)-5-(p-hydroxyphenyl)-, methyl carbonate (4CI) (CA INDEX NAME)



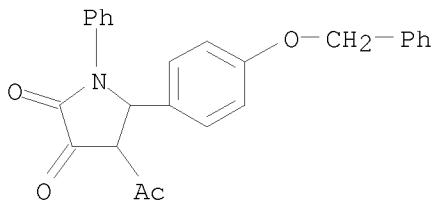
RN 861035-91-8 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-1-(6-butoxy-3-pyridinyl)-5-(4-hydroxyphenyl)- (CA INDEX NAME)



RN 861035-92-9 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-1-phenyl-5-[4-(phenylmethoxy)phenyl]- (CA INDEX NAME)



L3 ANSWER 65 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1938:30152 CAPLUS

DOCUMENT NUMBER: 32:30152

ORIGINAL REFERENCE NO.: 32:4166d-h

TITLE: Quinoline derivatives. III

AUTHOR(S): Ghosh, Tejendra N.

SOURCE: J. Indian Chem. Soc. (1937), 14, 713-16

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C. A. 31, 7431.8. In that the therapeutic value of ichthyoil oils has been attributed to the presence of alkylthiophenes and the replacement of the Ph group in the cinchophen mol. by the thiophene radical results in a product with marked antiphlogistic and analgesic properties it has seemed of interest to synthesize a compound in which the thiophene ring is fused with the quinoline residue. A mixture of 10.4 g. of Et 3,4-dihydroxythiophene-2,5-dicarboxylate and 7.5 g. PhNH<sub>2</sub> was heated on an oil bath for 30 min. and at 170-5° for 2.5 hrs. The product was triturated and washed with alc. and crystallized from dilute pyridine, yielding 8.5 g. of 2,5-diphenylcarbamido-3,4-dihydroxythiophene (I), C<sub>18</sub>H<sub>14</sub>N<sub>2</sub>O<sub>4</sub>S, m. 292-3° (decomposition). I (6 g.) was heated with 30 cc. concentrated H<sub>2</sub>SO<sub>4</sub> for 3 hrs. at 100° and the cooled reaction mixture was poured onto ice, treated with excess Na<sub>2</sub>CO<sub>3</sub>, filtered and acidified. The greenish white amorphous solid was recrystd. from hot H<sub>2</sub>O and gave 1.5 g. of 4-hydroxythiophene-2,3-(3',4')-2'-hydroxyquinolinesulfonic acid, C<sub>11</sub>H<sub>7</sub>N<sub>0</sub>S<sub>2</sub>, m. above 310°, forming HBr and HCl salts, both m. above 300°. Attempts were made to condense Et 1-N-phenyl-3,4-dihydroxypyrrolidine-2,5-dicarboxylate with PhNH<sub>2</sub> but no reaction was observed. Following the work of Narang and Ray (C. A. 25, 3342) on the synthesis of glyoxalinoquinolines as antimalarials, 13.2 g. of 2-methylbenzimidazazole was condensed with 7.3 g. (CO<sub>2</sub>Et)<sub>2</sub> in the presence of 2.3 g. Na in 100 cc. absolute alc. The mass was diluted with H<sub>2</sub>O and extracted

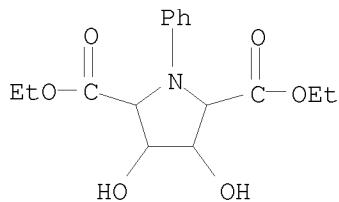
with Et<sub>2</sub>O. Acidification of the aqueous solution with excess dilute HCl and recrystn. of the washed precipitate from hot H<sub>2</sub>O gave 3 g. of 1,4-dibenzimidazolylbiacetyl (II), C<sub>18</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>, m. above 300°. Synthesis of bis(benzimidazolylquinoline) derivs. by condensation of II with o-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CHO in the presence of Ac<sub>2</sub>O and fused NaOAc and in pyridine in the presence of piperidine was not achieved even on continued refluxing.

IT 861035-94-1P, 2,5-Pyrrolidinedicarboxylic acid, 3,4-dihydroxy-1-phenyl-, diethyl ester

RL: PREP (Preparation)  
(preparation of)

RN 861035-94-1 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 3,4-dihydroxy-1-phenyl-, 2,5-diethyl ester (CA INDEX NAME)



L3 ANSWER 66 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1932:18264 CAPLUS

DOCUMENT NUMBER: 26:18264

ORIGINAL REFERENCE NO.: 26:1928a-e

TITLE: Pyrazopyrrolidones

AUTHOR(S): Dohrn, M.; Thiele, A.

SOURCE: Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen (1931), 64B, 2863-5

CODEN: BDCBAD; ISSN: 0365-9488

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB By condensation of primary or secondary amines with an aldehyde and  $\alpha, \gamma$ -diketonic acid mixture Schiff obtained diketopyrrolidines (I) with an RCO group on C atom 3. From the I there can be obtained, through ketonization of the enolic group in position 4, 4-hydrazone which are capable of again forming a ring, with the 3-RCO group, yielding a bicyclic system (II) of two 5-membered rings with two C atoms in common. This 2nd ring closure does not take place when the substituent on C atom 3 is RO<sub>2</sub>C instead of RCO. 2-Phenyl-3-acetyl-4,5-diketopyrrolidine, from BzH and saturated alc. NH<sub>3</sub> in benzene with AcCH<sub>2</sub>COCO<sub>2</sub>Et, m. 195-6°, gives a wine-red color with alc. FeCl<sub>3</sub>; phenylhydrazone, m. 217°. The latter, boiled in alc. containing a little concentrated H<sub>2</sub>SO<sub>4</sub>, condenses to 2,4-diphenyl-3-methylpyrazo-6-pyrrolidone, m. 214-5°. In the same way were obtained the following addnl. 3-methylpyrazo-6-pyrrolidones: 1,4-dimethyl-2-phenyl, m. 250-5°; 2-piperonyl-4-phenyl, m. 216-7°; 1,2,4-triphenyl, m. 158-9°; 1-mtolyl-2-p-methoxyphenyl-4-phenyl, m. 167-9°; 1-o-methoxyphenyl-2-p-methoxyphenyl-4-phenyl, m. 161-3°; 1,2-bis(p-methoxyphenyl)-4-phenyl, m. 162-40°; 1,2,3,4-tetraphenylpyrazo-6-pyrrolidone, m. 195-7°. These compds. were prepared from hydrazone of the following 3-acetyl-4,5-diketopyrrolidines: 1-methyl-2-phenyl, m. 215-60° (methylhydrazone, m. 204-5°); 2-piperonyl, m. 158-9°; 1,2-di-Ph, m. 229-310 (p-tolylhydrazone, m. 218° (decomposition)); 1-m-tolyl-2-p-methoxyphenyl, m. 186-8°; 1-o-methoxyphenyl-2-p-methoxyphenyl, turns brown 210°, m. 218-20°; 1,2-bis(p-methoxyphenyl), m. 163-40°.

IT 856099-62-2P, 2,3-Pyrrolidinedione, 4-acetyl-1-o-anisyl-5-p-anisyl-858450-37-0P, 2,3-Pyrrolidinedione, 4-acetyl-1,5-diphenyl-, 3-p-tolylhydrazone 858450-38-1P, 2,3-Pyrrolidinedione,

4-acetyl-1,5-di-p-anisyl- 858450-39-2P, 2,3-Pyrrolidinedione,

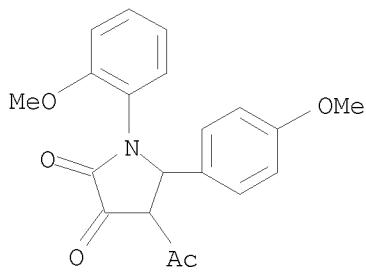
4-acetyl-5-p-anisyl-1-m-tolyl-

RL: PREP (Preparation)

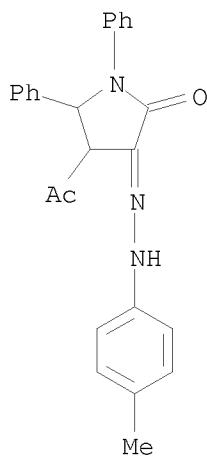
(preparation of)

RN 856099-62-2 CAPLUS

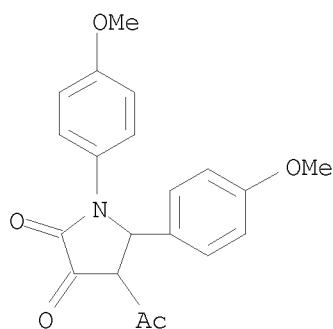
CN 2,3-Pyrrolidinedione, 4-acetyl-1-(2-methoxyphenyl)-5-(4-methoxyphenyl)- (CA INDEX NAME)



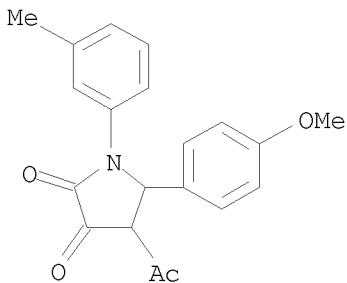
RN 858450-37-0 CAPLUS  
CN 2,3-Pyrrolidinedione, 4-acetyl-1,5-diphenyl-, 3-[2-(4-methoxyphenyl)hydrazone] (CA INDEX NAME)



RN 858450-38-1 CAPLUS  
CN 2,3-Pyrrolidinedione, 4-acetyl-1,5-bis(4-methoxyphenyl)- (CA INDEX NAME)



RN 858450-39-2 CAPLUS  
CN 2,3-Pyrrolidinedione, 4-acetyl-5-(4-methoxyphenyl)-1-(3-methylphenyl)- (CA INDEX NAME)



L3 ANSWER 67 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1925:3519 CAPLUS

DOCUMENT NUMBER: 19:3519

ORIGINAL REFERENCE NO.: 19:503e-i

TITLE: Interaction between ethyl ethylenemalonate and anilinophenylacetonitrile

AUTHOR(S): Higginbotham, Lucy; Lapworth, Arthur; Simpson, Charles

SOURCE: Journal of the Chemical Society, Transactions (1924), 125, 2339-44

CODEN: JCHTA3; ISSN: 0368-1645

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. Clarke and Lapworth, C. A. 1, 2116. The condensation of 25.5 g. PhCH(CN)NHPH and 22.8 g. MeCH:C(CO<sub>2</sub>Et)<sub>2</sub> in ice-cold EtOH by adding dropwise 6.85 g. KOH in an equal weight of H<sub>2</sub>O gives 19.5 g. of a precipitate

A, 5.8 g. of a yellow resin (after adding H<sub>2</sub>O) and, after heating on the H<sub>2</sub>O bath for several hrs., 10.5 g. of a resinous acid B. A was probably the K derivative of PhC[CHMeCH(CO<sub>2</sub>Et)<sub>2</sub>](CN)NHPH; boiled with 25% aqueous NaOH the steam

contained PhNH<sub>2</sub> and EtOH and the alkaline residue contained cyanide. With concentrated EtOH-KOH, NH<sub>3</sub> is evolved and cyanide formed; the Et<sub>2</sub>O-soluble acids

consisted almost wholly of I, below. Heated in aqueous Me<sub>2</sub>CO or in dilute AcOH,

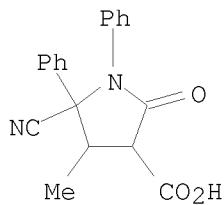
10 g. A gave about 6 g. Et 5-cyano-2-keto-1,5-diphenyl-4-methylpyrrolidine-3-carboxylate, m. 99°; it is repptd. unchanged from cold concentrated H<sub>2</sub>SO<sub>4</sub>; on heating it chars. It is not changed by boiling with dilute HCl but EtOH-H<sub>2</sub>SO<sub>4</sub> gives BzOEt. The free acid was obtained only as a resin (B above), softens 40° and completely liquid at 65°. Heating 2 hrs, with 50% KOH gives I. Boiling with HCl gives 5-cyano-2-keto-1,5-diphenyl-4-methylpyrrolidine, m. 111°; heated with an excess EtOH-KOH, it gives KCN, PhNH<sub>2</sub> and an oil from which I could be isolated. α-Benzoylethylmalonic acid (I), m. 164-5° (decomposition), was prepared in 1 step by condensing 20 g. PhCH(CN)NHPH and 18.6 g. MeCH:C(CO<sub>2</sub>Et)<sub>2</sub> in 75 cc. EtOH with 50% aqueous KOH (2.2 g.) and after 2 hrs. adding 45.5 g. KOH and boiling 2 hrs.; 18.5 g. Et<sub>2</sub>O-soluble oil was obtained, from which I crystallized. Heated at 160° I gives β-benzoylbutyric acid (II), m. 59-60°; semicarbazone, m. 177-8°. I was also synthesized from Ph α-bromoethyl ketone b4 110-2°, yellow oil with lachrymatory properties, and CH<sub>2</sub>CO<sub>2</sub>Et in C<sub>6</sub>H<sub>6</sub>. PhCH(CN)NMePh does not condense with MeCH:C(CO<sub>2</sub>Et)<sub>2</sub>; the action of alkali gives a yellow compound, m. 126-8°, which forms a HCl salt.

IT 861384-66-9P, 3-Pyrrolidinecarboxylic acid, 5-cyano-2-keto-4-methyl-1,5-diphenyl- 861582-70-9P, 3-Pyrrolidinecarboxylic acid, 5-cyano-2-keto-4-methyl-1,5-diphenyl-, ethyl ester

RL: PREP (Preparation)  
(preparation of)

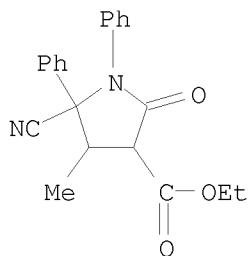
RN 861384-66-9 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 5-cyano-4-methyl-2-oxo-1,5-diphenyl- (CA INDEX NAME)



RN 861582-70-9 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 5-cyano-4-methyl-2-oxo-1,5-diphenyl-, ethyl ester (CA INDEX NAME)



L3 ANSWER 68 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1915:17111 CAPLUS

DOCUMENT NUMBER: 9:17111

ORIGINAL REFERENCE NO.: 9:2794i,2795a-d

TITLE: Diketopyrrolidine derivatives.

INVENTOR(S): Thiele, A.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 1148637	-----	19150803	US	-----

AB p-Methyl-diphenylbenzoyldiketopyrrolidine, crystalline m. 248° is made by heating p-toluidine with benzaldehyde in absolute alc., adding Et sodo benzoylepyrrolidine dissolved in absolute alc. and glacial HOAc, heating for 12 hrs. and precipitating with HCl, purifying through the Na salt and crystalline

from alc. 1-o-Tolyl-2-phenyl-3-acetyl-4,5-diketopyrrolidine, rose colored crystalline, m. 177-9°, is made by reaction in Et2O solution of o-toluidine and benzaldehyde on Et acetylpyrrolidine. 1-o-Methoxyphenyl-2-phenyl-3-acetyl-4,5-diketopyrrolidine, m. 225-7° (decomposition), is made by reaction in ether solution of anisidine, benzaldehyde and Et acetylpyrrolidine; 1-Phenyl-2-piperonyl-3-acetyl-4,5-diketopyrrolidine, m. 197°, by heating together aniline, piperonal and Et acetylpyrrolidine, in C6H6. 1-p-Tolyl-2-p-dimethylaminophenyl-3-acetyl-4,5-diketopyrrolidine, a brown powder, m. 166° (decomposition), is made by reaction in C6H6 of Et acetylpyrrolidine, p-toluidine and p-dimethylaminobenzaldehyde. 1-Quinolyl-2-phenyl-3-acetyl-4,5-diketopyrrolidine, m. 222° (decomposition), is made from

8-aminoquinoline, benzaldehyde and Et acetylpyroracetate in C6H6 solution 1-[1-Phenyl-2,3-dimethyl-5-pyrazolyl]-2-phenyl-3-acetyl-4,5-diketopyrrolidine, a light brown powder, with a bitter taste, decompose on heating, is made from phenyldimethylaminopyrazolone, benzaldehyde and Et acetyl pyroracetate, by heating in C6H6 at 100-10° for 5-6 hrs.

1-Phenyl-2-furfuryl-3-acetyl-4,5-diketopyrrolidine, yellow-green crystalline, soluble in alc. and ether and m. 190° (decomposition), is made by heating furfural, aniline and Et acetylpyroracetate in C6H6 on a H2O-bath for 2 hrs. 1-o-Methoxyphenyl-2-phenyl-3-benzoyl-4,5-diketopyrrolidine, crystalline m. 215-7° (decomposition), is made by reaction of o-anisidine, benzaldehyde and Et benzoylpyroracetate in C6H6 for 24 hrs. All these compds. are insol. in H2O, difficultly soluble in ether and C6H6, soluble in alkalies and stable when heated with dilute acids or alkalies. They are proposed for use as medicines.

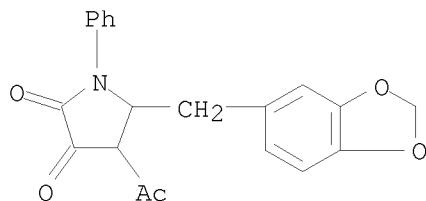
IT 859958-02-4P, 4,5-Pyrroledione, 3-acetyl-2,3-dihydro-1-phenyl-2-piperonyl 860759-80-4P, 4,5-Pyrroledione, 3-acetyl-2-p-dimethylaminophenyl-2,3-dihydro-1-p-tolyl- 860759-81-5P, 4,5-Pyrroledione, 3-acetyl-2,3-dihydro-2-phenyl-1-o-tolyl-

RL: PREP (Preparation)

(preparation of)

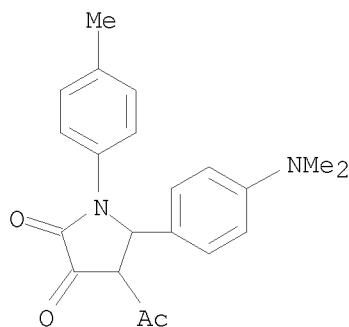
RN 859958-02-4 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-(1,3-benzodioxol-5-ylmethyl)-1-phenyl- (CA INDEX NAME)



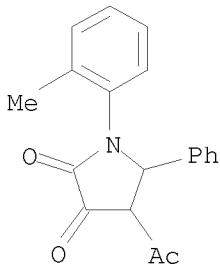
RN 860759-80-4 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-5-[4-(dimethylamino)phenyl]-1-(4-methylphenyl)- (CA INDEX NAME)



RN 860759-81-5 CAPLUS

CN 2,3-Pyrrolidinedione, 4-acetyl-1-(2-methylphenyl)-5-phenyl- (CA INDEX NAME)



L3 ANSWER 69 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1911:15334 CAPLUS

DOCUMENT NUMBER: 5:15334

ORIGINAL REFERENCE NO.: 5:2642f-i

TITLE: Synthesis of Pyrrole Compounds from Imido Acids.  
N-Phenyl- $\alpha$ - $\alpha$ '-Dicarbethoxy- $\beta$ , $\beta$ '-Diketopyrrolidine

AUTHOR(S): Johnson, Treat B.; Bengis, Robert

CORPORATE SOURCE: Sheffield Lab., Yale Univ.

SOURCE: Journal of the American Chemical Society (1911), 33, 745-55

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

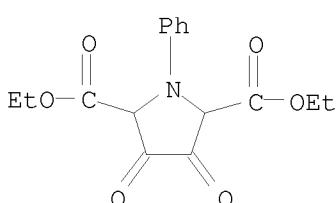
AB In presence of EtONa, each of the 4 combinations of diethyl or dimethyl oxalate and diethyl or dimethyl N-phenylglycolamide condense giving N-phenyl- $\alpha$ , $\alpha$ '-dicarbethoxy- $\beta$ , $\beta$ '-diketopyrrolidine, formula (I), needle-like prisms from hot alc. or AcOH, m. 137-8°. Similarly in MeONa the 4 combinations gave N-phenyl- $\alpha$ , $\alpha$ '-dicarbethoxy- $\beta$ , $\beta$ '-diketopyrrolidine, crystals from hot alc. m. 188-9°, and in some cases a trace of (I). Mouilpied (J. Chemical Society, 87, 435) under similar conditions obtained 6 products, these were probably mixtures of these 2 compds. The yellow disodium salt of (I) when digested in alc. with an excess of a halide of an aromatic base yields the colorless monosodium salt. Barium salt. H2O yellow. On digesting the disodium salt of (I) with nitrobenzyl chloride, 2 products were obtained.

(a) N-phenyl- $\alpha$ , $\alpha$ '-dicarbethoxy- $\alpha$ -p-nitrobenzyl- $\beta$ , $\beta$ '-diketopyrrolidine (II), orange colored powder from alc. + H2O, m. 180-2°, (b) the part insol. in alc. + H2O gave di-(p-nitrobenzyl)-N-phenyl- $\alpha$ , $\alpha$ '-dicarbethoxy- $\beta$ , $\beta$ '-diketopyrrolidine, yellow prisms from AcOH, m. 132°. HI or Al amalgam do not reduce (I).

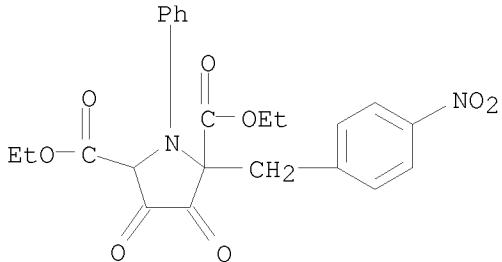
IT 859957-84-9, 2,5-Pyrrolidinedicarboxylic acid, 3,4-diketo-1-phenyl-, diethyl ester (and derivs.)

RN 859957-84-9 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 3,4-dioxo-1-phenyl-, 2,5-diethyl ester (CA INDEX NAME)



IT 860759-52-0P, 2,5-Pyrrolidinedicarboxylic acid,  
 3,4-diketo-2-(p-nitrobenzyl)-1-phenyl-, diethyl ester  
 RL: PREP (Preparation)  
 (preparation of)  
 RN 860759-52-0 CAPLUS  
 CN 2,5-Pyrrolidinedicarboxylic acid, 2-[(4-nitrophenyl)methyl]-3,4-dioxo-1-phenyl-, 2,5-diethyl ester (CA INDEX NAME)



L3 ANSWER 70 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1910:1764 CAPLUS  
 DOCUMENT NUMBER: 4:1764  
 ORIGINAL REFERENCE NO.: 4:319h-i,320a-i,321a-h  
 TITLE: Syntheses of Cinchonic Acid  
 AUTHOR(S): Borsche, W.  
 CORPORATE SOURCE: Gen. Chem. Inst.; Univ. Gottingen  
 SOURCE: Berichte der Deutschen Chemischen Gesellschaft (1910),  
 42, 4072-88  
 CODEN: BDCGAS; ISSN: 0365-9496  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable  
 OTHER SOURCE(S): CASREACT 4:1764

GI For diagram(s), see printed CA Issue.

AB  $\alpha, \beta, N$ -Triphenyl- $\alpha', \beta'$ -diketopyrrolidine, formula (I) below, is prepared from phenylpyruvic acid, BzH and PhNH<sub>2</sub>; colorless needles, m. 250°. Yield, 80%. It is also formed from the acid and benzalaniline. It does not react with ketone reagents. Acetate, crystalline powder, m. 185°. Benzoate, crystalline, m. 174°.  
 $\alpha, \beta, N$ -Triphenyl- $\alpha'$ -keto- $\beta'$ -hydroxypyrrrolidine (II) is produced from AcOH, Zn dust and (I); colorless crystals, m. 238°. Distillation decomposes it into stilbene, gases and a compound C<sub>21</sub>H<sub>17</sub>ON; needles, m. about 338°.  $\alpha, \beta$ -Diphenyl-N-o-tolyl- $\alpha', \beta'$ -diketopyrrolidine (III) is prepared in a similar manner to (I) by the use of o-toluidine; colorless, crystalline powder, m. 232-4°. m-Tolyl derivative, brittle, yellow resin. p-Tolyl compound, colorless crystals, m. 224°.  $\alpha, \beta$ -Diphenyl-N-m-nitrophenyl- $\alpha', \beta'$ -diketopyrrolidine (IV), from m-nitraniline; pale yellow needles, m. 226°.  $\beta, N$ -Diphenyl- $\alpha', \beta'$ -diketopyrrolidine, from PhNH<sub>2</sub> and HCHO; crystalline powder, m. about 208°.  $\beta, N$ -Diphenyl- $\alpha$ -p-nitrophenyl- $\alpha', \beta'$ -diketopyrrolidine, from PhNH<sub>2</sub>, and p-nitrobenzaldehyde; almost colorless crystals, m. 192°.  $\beta, N$ -Diphenyl- $\alpha$ ,o-hydroxyphenyl- $\alpha', \beta'$ -diketopyrrolidine, from PhNH<sub>2</sub> and salicylic aldehyde; colorless needles, m. 252°.  $\beta, N$ -Diphenyl- $\beta$ -p-methoxyphenyl- $\alpha', \beta'$ -diketopyrrolidine, colorless crystals, m. 195°. When distilled it gives p-methoxystilbene.  
 $\alpha, \beta$ -Diphenyl- $\beta$ -naphthoquinoline- $\gamma$ -carboxylic acid ( $\alpha, \beta$ -diphenyl- $\beta$ -naphthocinchonic acid) (V) is prepared from phenylpyruvic acid, BzH and  $\beta$ -naphthylamine; pale yellow, crystalline

powder, m. and evolves CO<sub>2</sub> about 275°. Yield, 40%. Sodium salt, hair-like needles.  $\alpha$ , $\beta$ -Diphenyl- $\beta$ -naphthoquinoline (VI), formed by heating the acid; colorless needles from acetone or AcOH + H<sub>2</sub>O, rhombic plates from AcOEt + alc., m. 179-80°.  $\alpha$ -Methyl- $\beta$ -phenyl- $\beta$ -naphthocinchonic acid (VII), from phenylpyruvic acid, AcH and  $\beta$ -naphthylamine; colorless, highly insol. needles. When heated it gives  $\beta$ -phenyl- $\beta$ -naphthoquinoline (VIII); yellow, pointed, acute-angled prisms with 1 H<sub>2</sub>O, m. 101°. Hydrochloride and sulphate, colorless needles. Nitrate, lustrous plates. All the salts have a deep blue fluorescence in solution, it is specially intense in the case of the sulphate.  $\beta$ -Phenyl- $\beta$ -naphthocinchonic acid (IX), from phenylpyruvic acid, HCHO and  $\beta$ -naphthylamine; colorless flocks. Yield, 22-5%. When heated it forms the quinoline derivative (X); needles with 2 H<sub>2</sub>O, m. and evolves gas 111°.  $\alpha$ ,N-Diphenyl- $\beta$ -o-nitrophenyl- $\alpha'$ , $\beta'$ -diketopyrrolidine (XI), from o-nitrophenylpyruvic acid, BzH and PhNH<sub>2</sub>; yellowish plates, m. and decomposes 207-8°. Yield, 150% of the nitro acid.

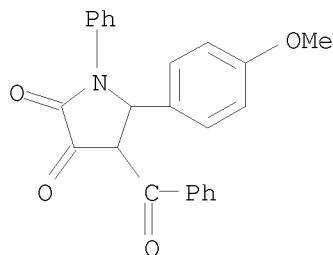
$\alpha$ -Phenyl- $\beta$ -o-nitroPhenyl- $\beta$ -naphthocinchonic acid (XII), from o-nitrophenylpyruvic acid, BzH and  $\beta$ -naphthylamine; crystalline. Yield, 33%. When fused it gives  $\alpha$ -phenyl- $\beta$ -o-nitrophenyl- $\beta$ -naphthoquinoline; yellow, rhombic plates which are stated to have 1 and also 0.5 mol. H<sub>2</sub>O, m. 193-4°. o-Nitrophenylpyruvic acid,  $\beta$ -naphthylamine and HCHO also form a naphthocinchonic acid. Yield, about 22%. Benzoylpyruvic acid, BzH and PhNH<sub>2</sub> give  $\alpha$ ,N-diphenyl- $\beta$ -benzoyl- $\alpha'$ , $\beta'$ -diketopyrrolidine (XIII); colorless needles, m. and darkens 242-4°. Anisic aldehyde forms the corresponding N-phenyl- $\alpha$ -p-methoxyphenyl- $\beta$ -benzoyl- $\alpha'$ , $\beta'$ -diketopyrrolidine; colorless crystals, m. 228°.

$\alpha$ -Phenyl- $\beta$ -benzoyl- $\beta$ -naphthocinchonic acid (XIV), from benzoylpyruvic acid, BzH and  $\beta$ -naphthylamine; colorless needles. Yield, 25%. When melted it gives the naphthoquinoline; colorless, slender, thickly felted needles, m. 185°.  $\beta$ -Benzoyl- $\beta$ -naphthocinchonic acid (XV), from benzoylpyruvic acid, HCHO and  $\beta$ -naphthylamine; pale yellow, crystalline powder. Yield, 34%. When m. it passes into the corresponding quinoline; colorless needles, m. 108-9°. Benzylpyruvic acid, BzH and PhNH<sub>2</sub> form N, $\alpha$ -diphenyl- $\beta$ -benzyl- $\alpha'$ , $\beta'$ -diketopyrrolidine (XVI); colorless needles, m. 196°. Yield, 100% of the acid.

$\alpha$ -Phenyl- $\beta$ -benzylcinchonic acid (XVII) is formed together with the preceding compound, from which it is separated by its solubility in aqueous Na<sub>2</sub>CO<sub>3</sub>; crystalline, m. 290°. Yield, 13%. When heated it gives  $\alpha$ -phenyl- $\alpha$ -benzylquinoline; colorless needles, m. 96-7°. 2-Methyl- $\alpha$ -phenyl- $\beta$ -benzylcinchonic acid (XVIII), from benzylpyruvic acid, BzH and m-toluidine; slender, colorless needles. Yield, about 35% of the acid. When fused it is converted into 2-methyl- $\alpha$ -phenyl- $\beta$ -benzylquinoline; needles, m. 99°. Benzylpyruvic acid, BzH and  $\beta$ -naphthylamine form  $\alpha$ -phenyl- $\beta$ -benzyl- $\beta$ -naphthocinchonic acid (XIX); pale yellow, crystalline powder. Yield, 57%. The corresponding naphthoquinoline is deposited in colorless needles, m. 152°. The following groups of quinoline- $\gamma$ -carboxylic acids may be synthesized by means of Dobner's reaction. (1)  $\alpha$ -Substituted  $\gamma$ -carboxylic acids from pyruvic acid, primary aromatic amines and homologues of HCHO. (2)  $\beta$ -Substituted (naphtho-) quinoline- $\gamma$ -carboxylic acids, from monosubstituted pyruvic acid, HCHO and  $\beta$ -naphthylamine. (3)  $\alpha$ , $\beta$ -Disubstituted  $\gamma$ -carboxylic acids from monosubstituted pyruvic acid, primary aromatic amines and the homologues of HCHO (cf. following abstract).

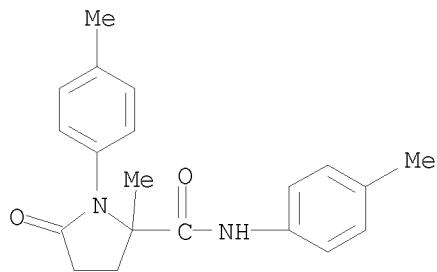
IT 859958-17-1P, 2,3-Pyrroledione, 5-p-anisyl-4-benzoyl-4,5-dihydro-1-phenyl-  
RL: PREP (Preparation)  
(preparation of)

RN 859958-17-1 CAPLUS  
CN 2,3-Pyrrolidinedione, 4-benzoyl-5-(4-methoxyphenyl)-1-phenyl- (CA INDEX  
NAME)

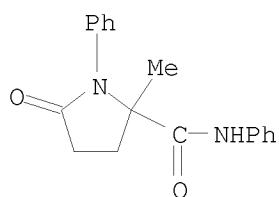


L3 ANSWER 71 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1909:14668 CAPLUS  
DOCUMENT NUMBER: 3:14668  
ORIGINAL REFERENCE NO.: 3:2696e-i,2697a-b  
TITLE: Phthaleinoximes  
AUTHOR(S): Meyer, Richard; Kissin, S. M.  
CORPORATE SOURCE: Chem. Lab., Techn. Hochsch., Brunswick  
SOURCE: Berichte der Deutschen Chemischen Gesellschaft (1909),  
42, 2825-38  
CODEN: BDCGAS; ISSN: 0365-9496  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable  
GI For diagram(s), see printed CA Issue.  
AB The constitution of the phthaleinoximes is discussed at considerable length; the results are expressed in the formulas given below. Benzoyl phenolphthaleinoxime, formula (I) below; colorless crystals, m. 175°. It is hydrolyzed with difficulty. The formula C<sub>20</sub>H<sub>15</sub>O<sub>3</sub>N for the reduction product of phenolphthaleinoxime is confirmed. Hydroquinolphthalein- $\alpha$ -oxime trimethyl ether, by the action of Me<sub>2</sub>SO<sub>4</sub>; needles, m. 123-4°. Triacetyl derivative, crystalline, m. 210°. Tribenzoyl derivative, needles, m. 226-7°. The  $\alpha$ -oxime (II) could not be reduced by means of Zn dust and NaOH, but the  $\beta$ -oxime (III), under these conditions, is converted into the  $\gamma$ -oxime (IV).  $\gamma$ -Oxime tribenzoyl derivative, yellow crystals, m. 275-80°, previously darkening. Hydroxyphenylphthalide oxime, colorless plates with 1 MeOH, m. 215-6°. Dibenzoyl derivative, colorless needles, m. 233-4°. Hydroxydiphenylphthalide oxime, colorless, cubical crystals from Et<sub>2</sub>O, m. 204-5°, previously darkening. From alc. the crystals are yellow, but become colorless in Et<sub>2</sub>O or when heated at 120°. Dibenzoyl derivative, colorless needles, m. 150-1°. Methylglutolactonic acid (V) does not yield an oxime, and it does not react with phenylhydrazine nor with bromophenylhydrazine (?); unsym. methylphenylhydrazine converts it into NH<sub>4</sub> methylglutolactonate. The following additional derivatives of this acid have been prepared. Dianilide, colorless needles, m. 205-6°. Di-p-toluide, colorless needles, m. 198-9°. The acid converts  $\alpha$ - and  $\beta$ -naphthylamine into  $\alpha$ - and  $\beta$ -dinaphthylamine respectively and it fails to react with the nitranilines and with m-toluylenediamine.  
IT 859957-85-0P, 2-Pyrrolidinecarboxy-p-toluide, 5-keto-2-methyl-1-p-tolyl- 860759-04-2P, 2-Pyrrolidinecarboxanilide, 5-keto-2-methyl-1-phenyl-  
RL: PREP (Preparation)  
(preparation of)  
RN 859957-85-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 2-methyl-N,1-bis(4-methylphenyl)-5-oxo- (CA INDEX NAME)



RN 860759-04-2 CAPLUS  
CN 2-Pyrrolidinecarboxamide, 2-methyl-5-oxo-N,1-diphenyl- (CA INDEX NAME)



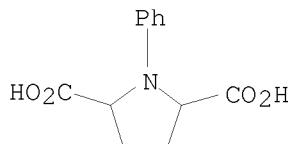
L3 ANSWER 72 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1909:10755 CAPLUS  
 DOCUMENT NUMBER: 3:10755  
 ORIGINAL REFERENCE NO.: 3:1992f-i,1993a  
 TITLE: Formation and Reactions of Imino Compounds. VIII. The formation of Methyl Derivatives of 2-Phenyl-1,3-Naphthalenediamine from the Three Tollylacetonitriles  
 AUTHOR(S): Best, S. R.; Thorpe, J. F.  
 SOURCE: Journal of the Chemical Society, Transactions (1909), 95, 261-73  
 CODEN: JCHTA3; ISSN: 0368-1645  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable  
 GI For diagram(s), see printed CA Issue.  
 AB By condensing o-tollylacetonitrile with 1 mol. Na, finely divided by melting and shaking in xylene and pouring off the solvent, and a trace of EtOH,  $\beta$ -imino- $\alpha$ -cyano- $\alpha$ , $\gamma$ -di-o-tollylpropane, MeC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>C(: NH)CH(CN)C<sub>6</sub>H<sub>4</sub>Me, is formed; viscous liquid, b13 270-80°. On washing the Et<sub>2</sub>O soluble of the above, after steam distillation, with dilute HCl, separating and treating with dilute Na<sub>2</sub>CO<sub>3</sub>, 6-amino-5-o-tollyl-2,4-di-o-methylbenzylpyrimidine, is secured. It separates from alc. in colorless needles, m. 1.40-1°. If this product is more desired than the first described the condensation can be carried out in an alc. soluble of NaOEt when it is obtained by filtering the soluble before distilling with steam. By treating the  $\beta$ -imino- $\alpha$ -cyano- $\alpha$ , $\gamma$ -di-o-tollylpropane with cold concentrate H<sub>2</sub>SO<sub>4</sub>, 6-o-tollyl-1-methyl-5,7-naphthalenediamine is formed; colorless plates, m. 136°. Dihydrochloride and diacetyl derivative Similarly, 6-amino-5-m-tollyl-2,4-di-m-methylbenzylpyrimidine, m. 147°; small needles, and  $\beta$ -imino- $\alpha$ -cyano- $\alpha$ , $\gamma$ -di-m-tollylpropane, b18 275-80° have been prepared. From the latter, by treatment with

H<sub>2</sub>SO<sub>4</sub>, 6-m-tolyl-2-methyl-5, 7-naphthylenediamine is made; small plates, m. 143°. This oxidizes by K<sub>3</sub>Cr<sub>2</sub>O<sub>7</sub> to 4-methylphthalic acid. Dihydrochloride and diacetyl derivative, also the pyrimidine hydrochloride. The corresponding p-pyrimidine; concentric needles, m. 117-20°. Hydrochloride,  $\beta$ -imino- $\alpha$ -cyano- $\alpha$ , $\gamma$ -di-p-tolylpropane, b<sub>18</sub> 280-83°. With H<sub>2</sub>SO<sub>4</sub> it yields 7-p-tolyl-2-methyl-6,8-naphthalenediamine; glistening plates, m. 160°. Dihydrochloride and diacetyl derivative. When the 3  $\beta$ -imino- $\alpha$  cyano- $\alpha$ , $\gamma$ -ditolylpropanes are treated with H<sub>2</sub>SO<sub>4</sub> the binding influence of a Me group in the m-position on the formation of the naphthalene ring at a certain C atom is clearly seen. The yield from compounds where the Me-group is in the m-position is only 10% while with the other 80% is obtained.

IT 859957-82-7, 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl-  
(and derivs., from adipic acid)

RN 859957-82-7 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl- (CA INDEX NAME)



L3 ANSWER 73 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1908:988 CAPLUS

DOCUMENT NUMBER: 2:988

ORIGINAL REFERENCE NO.: 2:278e-i,279a

TITLE: Condensation Products of Ethyl Levulinate, Hydrogen Cyanide and p-Substituted Anilines

AUTHOR(S): Weber, Hermann

CORPORATE SOURCE: Techn. Inst.; Univ. Berlin

SOURCE: Berichte der Deutschen Chemischen Gesellschaft (1908), 40, 4044-52

CODEN: BDCGAS; ISSN: 0365-9496

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

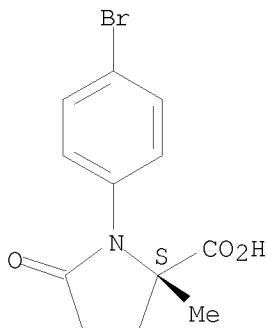
AB Ethyl levulinate, hydrogen cyanide and p-chloraniline yield 1-p-chlorophenyl-2-methylpyrrolidone-carboxylic nitrile, crystalline, m. 40-2°. Amide, prismatic needles, m. 207°. Acids, colorless needles, m. 179°. Barium salt, broad prisms with 1H<sub>2</sub>O. Methyl ester, crystalline. p-Bromaniline yields, similarly, the nitrile, slender, yellow needles, m. 49-51°. Amide, prismatic rods, m. 208°. Carboxylic acid, slender, colorless, interlaced needles, m. 189°. Silver salt, short prisms. Barium salt, short, prismatic needles with 1H<sub>2</sub>O. Methyl ester, short prisms. The nitrile is converted by NH<sub>2</sub>O.HCl into  $\gamma$ -hydroxyiminovaleric acid. The nitrile from p-iodoaniline is an oil. Amide, prismatic needles, m. 222°. Carboxylic acid, thin, colorless needles, m. 211-2°. Silver salt, short prisms, becoming brown on exposure to light. Methyl ester, brown, viscous oil. p-Aminobenzonitrile, treated in the same manner as the anilines, forms a crystalline compound, m. 77°. The yield is very small and no well defined derivatives could be prepared. Ethyl levulinate, hydrogen cyanide and ethyl p-aminobenzoate combine, forming the open chain derivative, EtO<sub>2</sub>CC<sub>6</sub>H<sub>4</sub>NHCMe(CN)CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et; crystalline, m. 75°. It is converted by HCl into the carboxylic acid, prisms with 1H<sub>2</sub>O m. 228-9°. Amide, crystalline, m. 149°. Amide from methyl p-aminobenzoate, crystalline, m. 171-2°.

IT 904813-38-3, Proline, 1-(p-bromophenyl)-5-keto-2-methyl-  
908578-57-4, Proline, 1-(p-chlorophenyl)-5-keto-2-methyl-  
908578-68-7, Proline, 1-(p-iodophenyl)-5-keto-2-methyl-  
(and derivs.)

RN 904813-38-3 CAPLUS

CN Proline, 1-(p-bromophenyl)-5-keto-2-methyl- (1CI) (CA INDEX NAME)

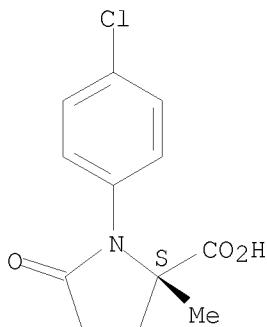
Absolute stereochemistry.



RN 908578-57-4 CAPLUS

CN Proline, 1-(p-chlorophenyl)-5-keto-2-methyl- (1CI) (CA INDEX NAME)

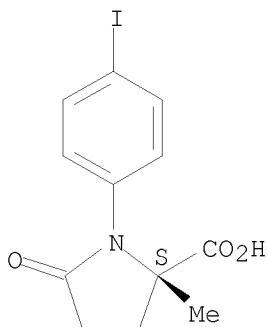
Absolute stereochemistry.



RN 908578-68-7 CAPLUS

CN Proline, 1-(p-iodophenyl)-5-keto-2-methyl- (1CI) (CA INDEX NAME)

Absolute stereochemistry.



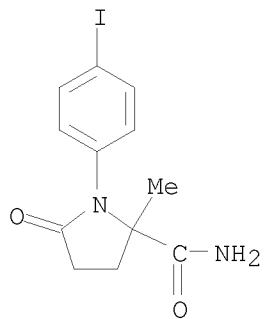
IT 859957-91-8P, 2-Pyrrolidinecarboxamide, 1-(p-iodophenyl)-5-keto-2-

methyl- 859957-93-0P, 2-Pyrrolidinecarboxamide,  
1-(p-chlorophenyl)-5-keto-2-methyl- 860759-08-6P,  
2-Pyrrolidinecarboxamide, 1-(p-carboxyphenyl)-5-keto-2-methyl-, methyl  
ester 860759-10-0P, 2-Pyrrolidinecarboxamide,  
1-(p-carboxyphenyl)-5-keto-2-methyl- 908578-59-6P, Proline,  
1-(p-carboxyphenyl)-5-keto-2-methyl-  
RL: PREP (Preparation)

(preparation of)

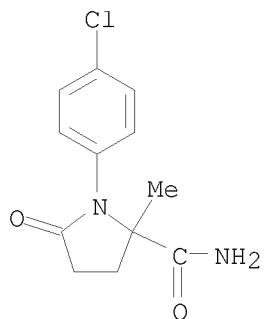
RN 859957-91-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 1-(4-iodophenyl)-2-methyl-5-oxo- (CA INDEX  
NAME)



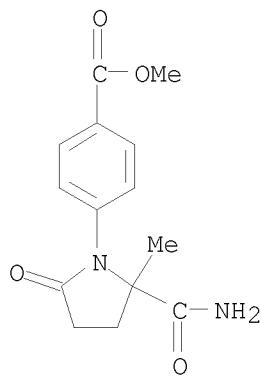
RN 859957-93-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 1-(4-chlorophenyl)-2-methyl-5-oxo- (CA INDEX  
NAME)



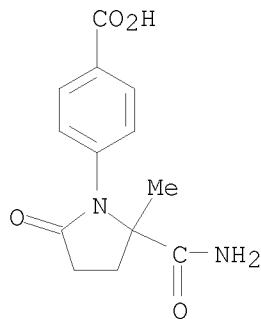
RN 860759-08-6 CAPLUS

CN Benzoic acid, 4-[2-(aminocarbonyl)-2-methyl-5-oxo-1-pyrrolidinyl]-, methyl  
ester (CA INDEX NAME)



RN 860759-10-0 CAPLUS

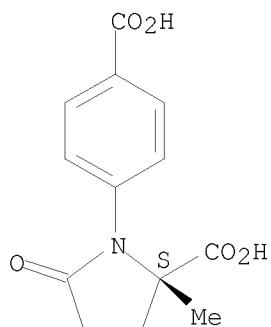
CN Benzoic acid, 4-[2-(aminocarbonyl)-2-methyl-5-oxo-1-pyrrolidinyl]- (CA INDEX NAME)



RN 908578-59-6 CAPLUS

CN Proline, 1-(p-carboxyphenyl)-5-keto-2-methyl- (1CI) (CA INDEX NAME)

Absolute stereochemistry.



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=> FIL STNGUIDE  
COST IN U.S. DOLLARS  
FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
115.41	303.31

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL
CA SUBSCRIBER PRICE	-16.80	-16.80

FILE 'STNGUIDE' ENTERED AT 17:32:42 ON 24 APR 2008  
 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT  
 COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.  
 LAST RELOADED: Apr 18, 2008 (20080418/UP).

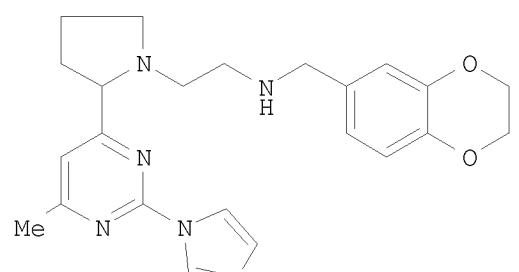
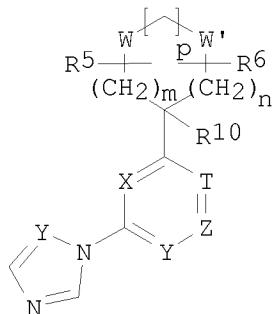
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L3 ANSWER 32 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2006:510936 CAPLUS  
 DOCUMENT NUMBER: 145:8185  
 TITLE: Preparation of heterocyclic inhibitors of inducible nitric oxide synthase dimerization for therapeutic use  
 INVENTOR(S): Gahman, Timothy C.; Lang, Hengyuan; Herbert, Mark R.; Thayer, Angelina M.; Hassig, Christian A.; Noble, Stewart A.; Cousins, Russell D.; Zhuang, Hui; Santos, Christopher R.; Chen, Xiaohong  
 PATENT ASSIGNEE(S): Kalypsys, Inc., USA  
 SOURCE: U.S. Pat. Appl. Publ., 108 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060116515	A1	20060601	US 2005-288888	20051128
AU 2005311985	A1	20060608	AU 2005-311985	20051128
CA 2589433	A1	20060608	CA 2005-2589433	20051128
WO 2006060424	A2	20060608	WO 2005-US43190	20051128
WO 2006060424	A3	20070329		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1817030	A2	20070815	EP 2005-852447	20051128
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
IN 2007KN01890	A	20070810	IN 2007-KN1890	20070525
KR 2007084574	A	20070824	KR 2007-711898	20070525
CN 101123962	A	20080213	CN 2005-80040524	20070525
PRIORITY APPLN. INFO.:			US 2004-631971P	P 20041201
			US 2005-672001P	P 20050414

OTHER SOURCE(S) :  
GI

MARPAT 145:8185



T

II

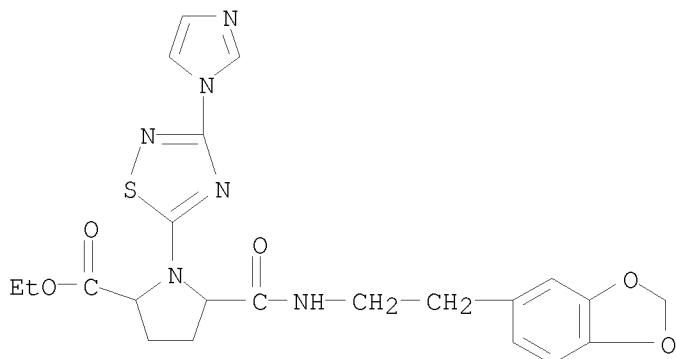
AB The present invention relates to compds. and methods useful as inhibitors of inducible nitric oxide synthase dimerization. Certain compds. of the subject invention have the following structural formula I: wherein T, V, X, and Y = CR4 and N; Z = CR3 and N; V = CR4 and N; W and W' = CH2, CR7R8, NR9, O, NO, S(O)q and CO; n, m and p = 0-5; q = 0-2; R3, R4, R10 = H, halogen, optionally substituted alkyl, haloalkoxy, etc.; and R7, R8, and R9 = H, halogen, optionally substituted alkyl, optionally substituted aralkyl, etc. Other compds. of the subject invention have structural formulas as defined in the invention. Also disclosed herein are pharmaceutical compns. comprising the compds. of the subject invention. The compds. of the invention can be used to inhibit or modulate NO synthesis and/or to lower NO levels in a patient. The preparation of the compds. is exemplified. For example, II was prepared from 2-[2-(2-imidazol-1-yl-6-methylpyrimidin-4-yl)pyrrolidin-1-yl]ethylamine and 2,3-dihydrobenzo[1,4]dioxin-6-carboxaldehyde. In HEK293 cells transiently transfected with human iNOS, II had an EC50 of <1 $\mu$ M.

IT 888312-95-6P, 5-[(2-(Benzodioxol-5-yl)ethyl]carbamoyl]-1-[3-(imidazol-1-yl)-[1,2,4]thiadiazol-5-yl]pyrrolidine-2-carboxylic acid ethyl ester 888312-96-7P 888312-97-8P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

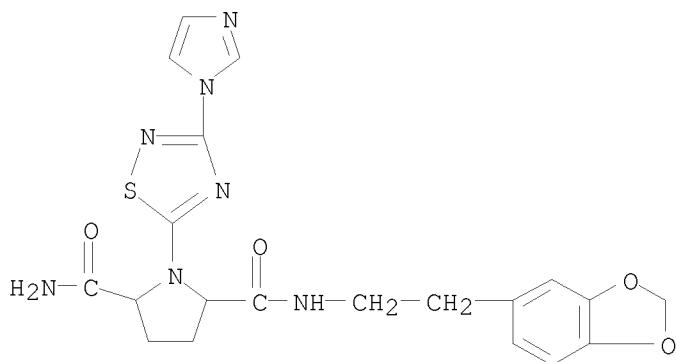
(drug candidate; preparation of heterocyclic inhibitors of inducible nitric oxide synthase dimerization for therapeutic use)

RN 888312-95-6 CAPLUS

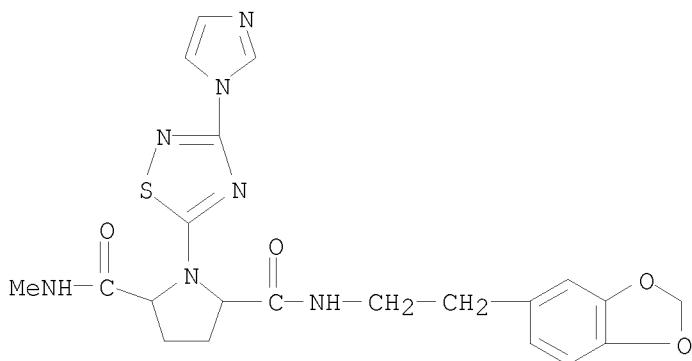
CN Proline, 5-[[2-(1,3-benzodioxol-5-yl)ethyl]amino]carbonyl]-1-[3-(1H-imidazol-1-yl)-1,2,4-thiadiazol-5-yl]-, ethyl ester (CA INDEX NAME)



RN 888312-96-7 CAPLUS  
CN 2,5-Pyrrolidinedicarboxamide, N2-[2-(1,3-benzodioxol-5-yl)ethyl]-1-[3-(1H-imidazol-1-yl)-1,2,4-thiadiazol-5-yl]- (CA INDEX NAME)

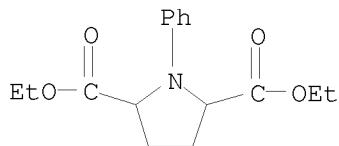


RN 888312-97-8 CAPLUS  
CN 2,5-Pyrrolidinedicarboxamide, N2-[2-(1,3-benzodioxol-5-yl)ethyl]-1-[3-(1H-imidazol-1-yl)-1,2,4-thiadiazol-5-yl]-N5-methyl- (CA INDEX NAME)



L3 ANSWER 33 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2006:359359 CAPLUS  
Correction of: 2005:1110275  
DOCUMENT NUMBER: 145:471313  
Correction of: 143:346991  
TITLE: Product class 10:  $\gamma$ -Lactams and larger ring lactams  
AUTHOR(S): Smith, M. B.  
CORPORATE SOURCE: Germany  
SOURCE: Science of Synthesis (2005), 21, 647-711  
CODEN: SSCYJ9  
PUBLISHER: Georg Thieme Verlag  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
AB A review of the preparation of  $\gamma$ -lactams and larger ring lactams focusing on the use of acyclic and cyclic precursors.  
IT 910810-49-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of  $\gamma$ -lactams and larger ring lactams)  
RN 910810-49-0 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-phenyl-, 2,5-diethyl ester (CA INDEX NAME)



L3 ANSWER 34 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:15992 CAPLUS

DOCUMENT NUMBER: 144:253959

TITLE: Scandium triflate catalyzed cycloaddition of imines with 1,1-cyclopropanediesters: efficient and diastereoselective synthesis of multisubstituted pyrrolidines

AUTHOR(S): Kang, Yan-Biao; Tang, Yong; Sun, Xiu-Li

CORPORATE SOURCE: State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China

SOURCE: Organic & Biomolecular Chemistry (2006), 4(2), 299-301

CODEN: OBCRAK; ISSN: 1477-0520

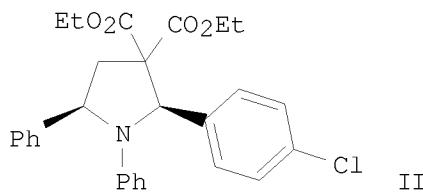
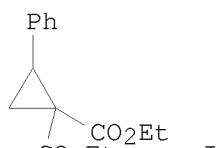
PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:253959

GI



AB A tandem ring-opening-cyclization reaction of cyclopropanes with imines in the presence of 5 mol% of scandium triflate was developed for the highly diastereoselective synthesis of multisubstituted pyrrolidines. E.g., reaction of 1,1-cyclopropane diester I with PhN:CHC6H4Cl-4, catalyzed by scandium triflate, gave the *cis* isomer of pyrrolidine II.

IT 877035-09-1P

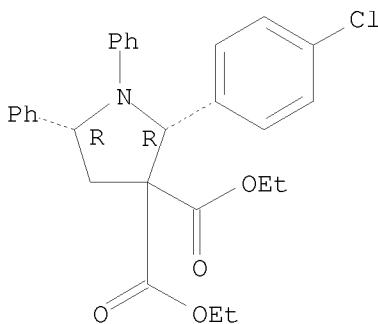
RL: SPN (Synthetic preparation); PREP (Preparation)

(diastereoselective synthesis of multisubstituted pyrrolidines by scandium triflate catalyzed cycloaddn. of imines with 1,1-cyclopropane diesters)

RN 877035-09-1 CAPLUS

CN 3,3-Pyrrolidinedicarboxylic acid, 2-(4-chlorophenyl)-1,5-diphenyl-, 3,3-diethyl ester, (2R,5R)-rel- (CA INDEX NAME)

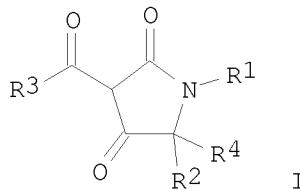
Relative stereochemistry.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 35 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2006:2507 CAPLUS  
 DOCUMENT NUMBER: 144:412355  
 TITLE: Method of preparation 3-acylpyrrolidine-2,4-dione compounds as herbicides  
 INVENTOR(S): Yang, Huazheng; Zhu, Youquan; Zou, Xiaomao; Hu, Fangzhong; Liu, Bin; Yang, Xiufeng  
 PATENT ASSIGNEE(S): Nankai University, Peop. Rep. China  
 SOURCE: Faming Zhuanli Shengqing Gongkai Shuomingshu, 22 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Chinese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1676515	A	20051005	CN 2005-10013206	20050317
PRIORITY APPLN. INFO.:			CN 2005-10013206	20050317
OTHER SOURCE(S):	CASREACT 144:412355; MARPAT 144:412355			
GI				



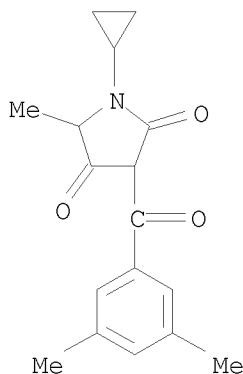
AB 3-Acylpyrrolidine-2,4-dione compds. I [R1= H, alkyl, alkoxyalkyl, haloalkyl, haloalkoxyalkyl, alkoxy carbonyl, alkenyl, haloalkenyl, substituted Ph, phenylalkyl; R2, R4= H, alkyl, alkoxy, phenylalkoxy, hydroxyalkyl, alkoxyalkyl, alkoxy carbonyl, haloalkyl, cyano; R3= H, alkyl, alkoxyalkyl, substituted heterocyclic, heterocyclic Ph, heterocyclic alkyl, heterocyclic alkoxy, heterocyclic alkylphenyl, Ph, phenoxyphenyl, phenylalkyl, aryl] useful as herbicides is prepared by treating substituted benzoylethyl acetate with Et N-substituted glycinate (at mole ratio of 1:1.5-3.0) at 60-100°C for 10-48 h, cooling to room temperature, adding sodium methoxide solution, and reacting at room temperature for 20-60 h.  
 IT 884493-97-4P  
 RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN

(Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of acylpyrrolidine dione derivative as herbicides)

RN 884493-97-4 CAPLUS

CN 2,4-Pyrrolidinedione, 1-cyclopropyl-3-(3,5-dimethylbenzoyl)-5-methyl- (CA INDEX NAME)



L3 ANSWER 36 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1300785 CAPLUS

DOCUMENT NUMBER: 145:27790

TITLE: Synthesis, properties, and antimicrobial activity of 3-hydrazone of 1-aryl-5-methyl-1,5-ethoxycarbonylpyrrolidine-2,3-diones

AUTHOR(S): Gein, V. L.; Gein, L. F.; Chirkova, M. V.; Mikhalev, V. A.; Voronina, E. V.

CORPORATE SOURCE: Perm State Pharmaceutical Academy, Perm, Russia

SOURCE: Pharmaceutical Chemistry Journal (2005), 39(8), 413-417

CODEN: PCJOAU; ISSN: 0091-150X

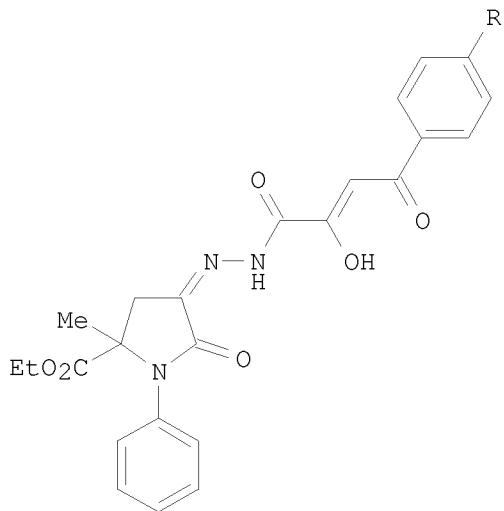
PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 145:27790

GI



I

AB Reactions of 5-methyl-1-aryl-ethoxycarbonylpyrrolidine-2,3-diones with hydrazine hydrate, phenylhydrazine, isoniazid, benzoylhydrazine, and thiosemicarbazide were used to synthesize a series of corresponding 3-hydrazone. All target products were obtained with a yield of 51 - 90%. The reactions of 3-hydrazone of 1-phenyl-5-methyl-5-ethoxycarbonylpyrrolidine-2,3-dione with 5-aryl-2,3-dihydro-2,3-furandiones yielded 3-N-aryloylpyruvylhydrazones of 5-methyl-1-phenyl-5-ethoxycarbonylpyrrolidine-2,3-dione I (R = H or Me). The condensation of 3-hydrazone of 5-methyl-1-(4-chlorophenyl)-5-ethoxycarbonylpyrrolidine-2,3-dione with 4-methoxybenzaldehyde led to the 5-methyl-3-N-4-methoxybenzylidene-hydrazino-1-(4-chlorophenyl)-5-ethoxycarbonyl-3-pyrrolidin-2-one. The synthesized compds. were characterized by physicochem. consts. and the parameters of IR and 1H NMR spectra. Some compds. were tested for antimicrobial activity.

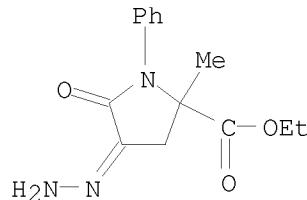
IT 889101-11-5P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(preparation and antimicrobial activity of aroyl(pyruvoyl)hydrazones of (phenyl)ethoxycarbonyl(pyrrolidine)dione via its condensation with hydrazine followed by condensation with aryl(dihydro)furanones)

RN 889101-11-5 CAPLUS

CN Proline, 4-hydrazoneo-2-methyl-5-oxo-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



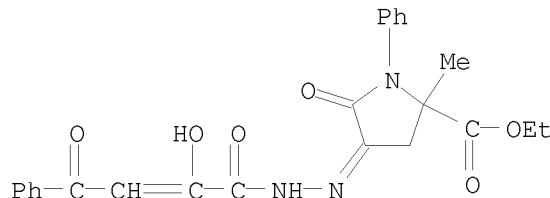
IT 889101-23-9P 889101-24-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and antimicrobial activity of aroyl(pyruvoyl)hydrazones of (phenyl)ethoxycarbonyl(pyrrolidine)dione via its condensation with hydrazine followed by condensation with aryl(dihydro)furanones)

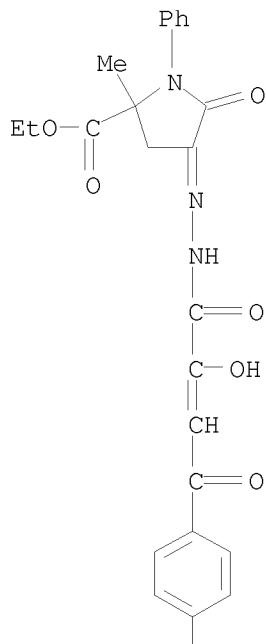
RN 889101-23-9 CAPLUS

CN Proline, 4-[(2-hydroxy-1,4-dioxo-4-phenyl-2-butenyl)hydrazone]-2-methyl-5-oxo-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 889101-24-0 CAPLUS

CN Proline, 4-[(2-hydroxy-4-(4-methylphenyl)-1,4-dioxo-2-butenyl]hydrazone]-2-methyl-5-oxo-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

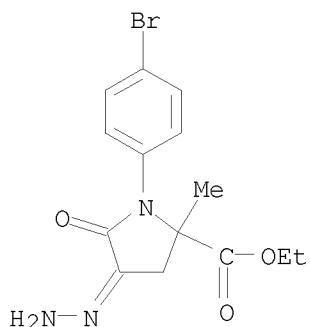


IT 889101-13-7P 889101-14-8P 889101-15-9P  
 889101-19-3P 889101-22-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL  
 (Biological study); PREP (Preparation)  
 (preparation and antimicrobial activity of hydrazones of  
 (aryl)ethoxycarbonyl(pyrrolidine)diones via their condensation with  
 substituted hydrazines)

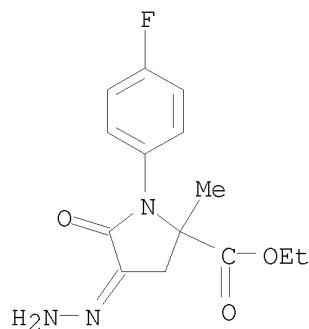
RN 889101-13-7 CAPLUS

CN Proline, 1-(4-bromophenyl)-4-hydrazono-2-methyl-5-oxo-, ethyl ester (9CI)  
 (CA INDEX NAME)

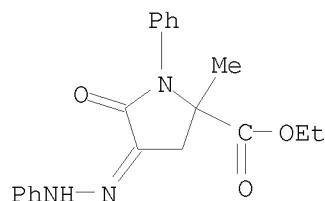


RN 889101-14-8 CAPLUS

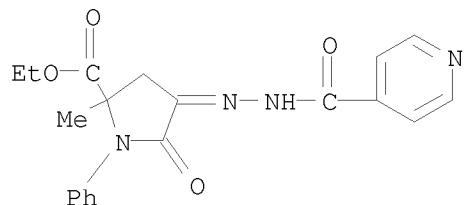
CN Proline, 1-(4-fluorophenyl)-4-hydrazono-2-methyl-5-oxo-, ethyl ester (9CI)  
(CA INDEX NAME)



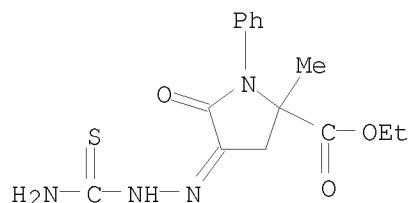
RN 889101-15-9 CAPLUS  
CN Proline, 2-methyl-5-oxo-1-phenyl-4-(phenylhydrazono)-, ethyl ester (9CI)  
(CA INDEX NAME)



RN 889101-19-3 CAPLUS  
CN 4-Pyridinecarboxylic acid, 2-[5-(ethoxycarbonyl)-5-methyl-2-oxo-1-phenyl-3-pyrrolidinylidene]hydrazide (CA INDEX NAME)



RN 889101-22-8 CAPLUS  
CN Proline, 4-[ (aminothioxomethyl)hydrazono]-2-methyl-5-oxo-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

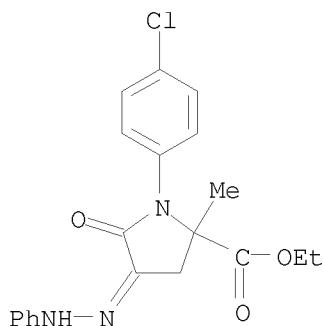


IT 889101-16-0P 889101-17-1P 889101-18-2P  
889101-20-6P 889101-21-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and antimicrobial activity of hydrazones of  
(aryl)ethoxycarbonyl(pyrrolidine)diones via their condensation with  
substituted hydrazines)

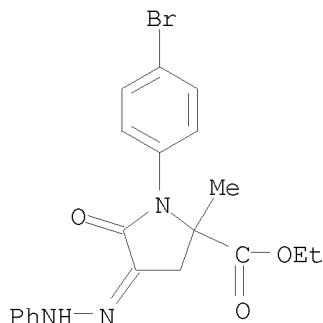
RN 889101-16-0 CAPLUS

CN Proline, 1-(4-chlorophenyl)-2-methyl-5-oxo-4-(phenylhydrazone)-, ethyl  
ester (9CI) (CA INDEX NAME)



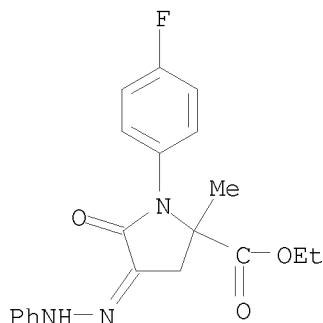
RN 889101-17-1 CAPLUS

CN Proline, 1-(4-bromophenyl)-2-methyl-5-oxo-4-(phenylhydrazone)-, ethyl  
ester (9CI) (CA INDEX NAME)



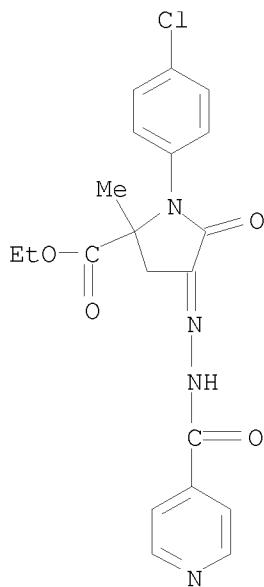
RN 889101-18-2 CAPLUS

CN Proline, 1-(4-fluorophenyl)-2-methyl-5-oxo-4-(phenylhydrazone)-, ethyl  
ester (9CI) (CA INDEX NAME)

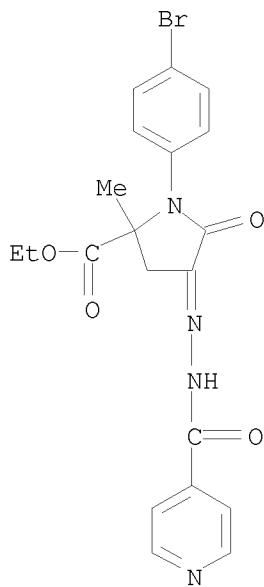


RN 889101-20-6 CAPLUS

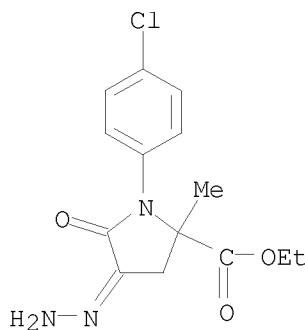
CN 4-Pyridinecarboxylic acid, 2-[1-(4-chlorophenyl)-5-(ethoxycarbonyl)-5-  
methyl-2-oxo-3-pyrrolidinylidene]hydrazide (CA INDEX NAME)



RN 889101-21-7 CAPLUS  
 CN 4-Pyridinecarboxylic acid, 2-[1-(4-bromophenyl)-5-(ethoxycarbonyl)-5-methyl-2-oxo-3-pyrrolidinylidene]hydrazide (CA INDEX NAME)



IT 889101-12-6P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and antimicrobial activity of methoxy(benzylidene)hydrazone of (chlorophenyl)ethoxycarbonyl(pyrrolidine)dione via its condensation with hydrazine followed by condensation with (methoxy)benzaldehyde)  
 RN 889101-12-6 CAPLUS  
 CN Proline, 1-(4-chlorophenyl)-4-hydrazono-2-methyl-5-oxo-, ethyl ester (9CI)  
 (CA INDEX NAME)



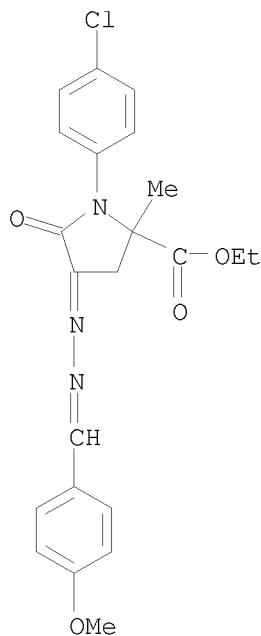
IT 889101-25-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and antimicrobial activity of methoxy(benzylidene)hydrazone of (chlorophenyl)ethoxycarbonyl(pyrrolidine)dione via its condensation with hydrazine followed by condensation with (methoxy)benzaldehyde)

RN 889101-25-1 CAPLUS

CN Proline, 1-(4-chlorophenyl)-4-[(4-methoxyphenyl)methylene]hydrazono]-2-methyl-5-oxo-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 37 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1269350 CAPLUS

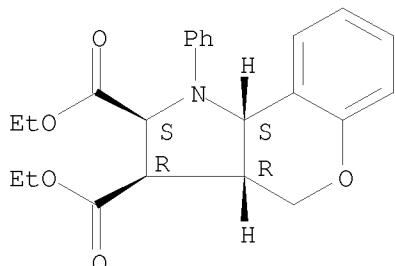
DOCUMENT NUMBER: 145:8053

TITLE: Intramolecular 1,3-dipolar cycloaddition of azomethine ylides generated from ethoxycarbonyl carbenoids and Schiff bases

AUTHOR(S): Khlebnikov, A. F.; Novikov, M. S.; Kostikov, R. R.; Kopf, J.

CORPORATE SOURCE: St. Petersburg State University, St. Petersburg,  
 198504, Russia  
 SOURCE: Russian Journal of Organic Chemistry (2005), 41(9),  
 1341-1348  
 CODEN: RJOCEQ; ISSN: 1070-4280  
 PUBLISHER: Pleiades Publishing, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 145:8053  
 AB Decomposition of Et diazoacetate in the presence of copper, copper acetylacetone, or copper trifluoroacetylacetone and Et 4-(2-iminophenoxyethyl)-2-butenoates leads to formation of chromeno[4,3-b]pyrrole-2,3-dicarboxylic acid derivs. The reactions involve intermediate formation of azomethine ylides which undergo regio- and stereoselective intramol. cycloaddn. at the C:C bond to afford chromeno[4,3-b]pyrroles. The steric structure of the product depends on the configuration of intermediate ylide and nature of the substituent at the ylide nitrogen atom.  
 IT 887764-58-1P  
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (mol. structure; preparation of chromenopyrroles by stereoselective intramol. 1,3-dipolar cycloaddn. of azomethine ylides from ethoxycarbonyl carbenoids and Schiff bases)  
 RN 887764-58-1 CAPLUS  
 CN [1]Benzopyrano[4,3-b]pyrrole-2,3-dicarboxylic acid, 1,2,3,3a,4,9b-hexahydro-1-phenyl-, 2,3-diethyl ester, (2R,3S,3aS,9bR)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT  
 L3 ANSWER 38 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:1163314 CAPLUS  
 DOCUMENT NUMBER: 144:88103  
 TITLE: Asymmetric Synthesis of Multifunctionalized Pyrrolines by a Ruthenium Porphyrin-Catalyzed Three-Component Coupling Reaction  
 AUTHOR(S): Xu, Hai-Wei; Li, Gong-Yong; Wong, Man-Kin; Che, Chi-Ming  
 CORPORATE SOURCE: Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, Shanghai Institute of Organic Chemistry, The Chinese Academy of Science, Shanghai, 200032, Peop. Rep. China  
 SOURCE: Organic Letters (2005), 7(24), 5349-5352  
 CODEN: ORLEF7; ISSN: 1523-7060  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:88103

AB Chiral multifunctionalized pyrrolines have been synthesized by a ruthenium porphyrin catalyzed three-component coupling reaction. In a one-pot reaction, ruthenium porphyrins catalyzed in situ generation of chiral azomethine ylides from chiral diazo esters and imines. Asym. 1,3-dipolar cycloaddn. reactions of the chiral azomethine ylides with dipolarophiles afforded the pyrrolines in good yields and high diastereoselectivity (up to 92% de).

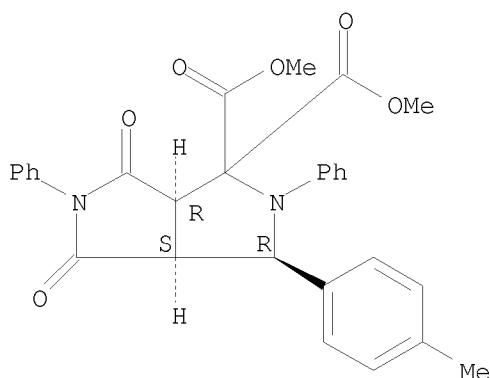
IT 871947-09-0P 872321-71-6P 872321-72-7P  
872321-73-8P 872321-74-9P 872321-75-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(asym. synthesis of multifunctionalized pyrrolines by a ruthenium porphyrin-catalyzed three-component coupling reaction)

RN 871947-09-0 CAPLUS

CN Pyrrolo[3,4-c]pyrrole-1,1(2H)-dicarboxylic acid, hexahydro-3-(4-methylphenyl)-4,6-dioxo-2,5-diphenyl-, 1,1-dimethyl ester,  
(3R,3aS,6aR)-rel- (CA INDEX NAME)

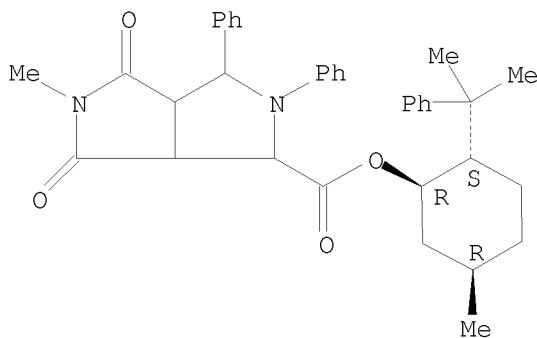
Relative stereochemistry.



RN 872321-71-6 CAPLUS

CN Pyrrolo[3,4-c]pyrrole-1-carboxylic acid, octahydro-5-methyl-4,6-dioxo-2,3-diphenyl-, (1R,2S,5R)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyl ester  
(CA INDEX NAME)

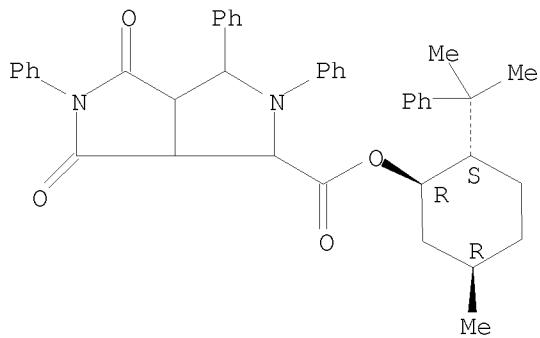
Absolute stereochemistry.



RN 872321-72-7 CAPLUS

CN Pyrrolo[3,4-c]pyrrole-1-carboxylic acid, octahydro-4,6-dioxo-2,3,5-triphenyl-, (1R,2S,5R)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyl ester  
(CA INDEX NAME)

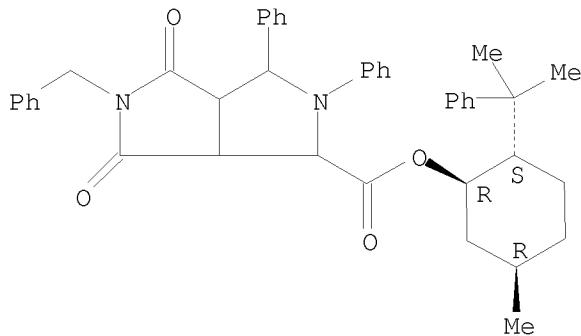
Absolute stereochemistry.



RN 872321-73-8 CAPLUS

CN Pyrrolo[3,4-c]pyrrole-1-carboxylic acid, octahydro-4,6-dioxo-2,3-diphenyl-5-(phenylmethyl)-, (1R,2S,5R)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyl ester (CA INDEX NAME)

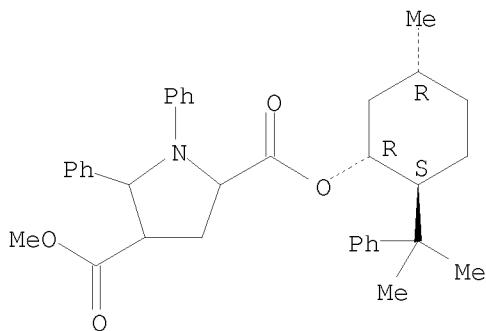
Absolute stereochemistry.



RN 872321-74-9 CAPLUS

CN 2,4-Pyrrolidinedicarboxylic acid, 1,5-diphenyl-, 4-methyl-2-[(1R,2S,5R)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyl] ester (CA INDEX NAME)

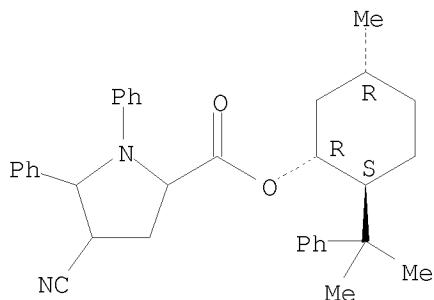
Absolute stereochemistry.



RN 872321-75-0 CAPLUS

CN Proline, 4-cyano-1,5-diphenyl-, (1R,2S,5R)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

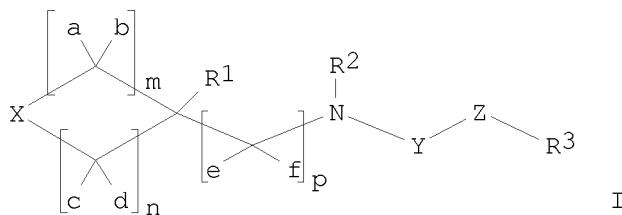


REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

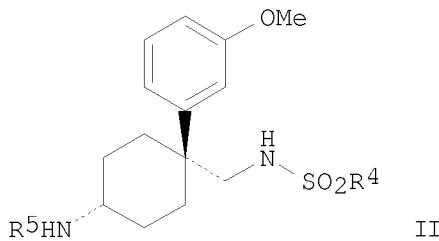
L3 ANSWER 39 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:1123880 CAPLUS  
 DOCUMENT NUMBER: 143:405923  
 TITLE: Preparation of heterocycle- and benzene-containing sulfonamide derivatives as LDL receptor agonists  
 INVENTOR(S): Ban, Hitoshi; Asano, Shigehiro  
 PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 233 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005097738	A1	20051020	WO 2005-JP6977	20050404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1736467	A1	20061227	EP 2005-728832	20050404
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRIORITY APPLN. INFO.:			JP 2004-112503	A 20040406
			WO 2005-JP6977	W 20050404

OTHER SOURCE(S): MARPAT 143:405923  
 GI



I



II

AB Enhancers for expression of low d. lipoprotein receptor containing the title compds. represented by the formula (I), prodrugs thereof, and their pharmaceutically acceptable salts [m, n, p = 0-4 and  $3 \leq m+n \leq 8$ ;  
 $X = O, S$ , each (un)substituted NH or CH<sub>2</sub>; R<sub>1</sub>-R<sub>3</sub> = H, each (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, arylcarbonyl, heteroarylcarbonyl, arylsulfonyl, heteroarylsulfonyl, arylalkyl, or heteroarylalkyl; Y = SO<sub>2</sub>, optionally esterified P(O)(OH), CO; Z = O, S, (un)substituted NH, (CH<sub>2</sub>)<sub>q</sub>; q = 0-4; a, b, c, d, e, f = H, HO, each (un)substituted alkyl, alkoxy, alkoxy carbonyl, aryl, heteroaryl, arylcarbonyl, heteroarylcarbonyl, arylalkyl, heteroarylalkyl, arylalkyloxy, or heteroarylalkyloxy; or one or plural combination(s) of a and b, c and d, or e and f represent oxo; e and f represent thioxo; a and c represent alkylene] are disclosed. Drugs for treating hyperlipemia and arteriosclerosis containing the compds. I are also disclosed. Thus, a solution of 40 mg tert-Bu [[[2-[cis-4-amino-1-(3-methoxyphenyl)cyclohexyl]methyl]amino]sulfonyl]carbamate and 22.0 mg 1-benzyl-4-piperidone in 2 mL 1,2-dichloroethane was treated with 71.7 mg sodium triacetoxylborohydride and stirred overnight, followed by treatment of the product with CF<sub>3</sub>CO<sub>2</sub>H in CH<sub>2</sub>Cl<sub>2</sub> to give N-[[cis-4-[(1-benzylpiperidin-4-yl)amino]-1-(3-methoxyphenyl)cyclohexyl]methyl]sulfonamide (II) (R<sub>4</sub> = NH<sub>2</sub>, R<sub>5</sub> = 1-benzyl-4-piperidinyl) (III). III and II (R<sub>4</sub> = Me, R<sub>5</sub> = 1,1'-biphenyl-4-ylmethyl) at 10  $\mu$ M increased the uptake of 1,1'-dioctadecyl-3,3',3'-tetramethylindocarbocyanine perchlorate (Dil)-labeled human low d. lipoprotein in HepG2 cells by 230 and 238%, resp.

IT 850887-29-5P, Diethyl cis-1-(2-methoxyphenyl)pyrrolidine-2,5-dicarboxylate

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

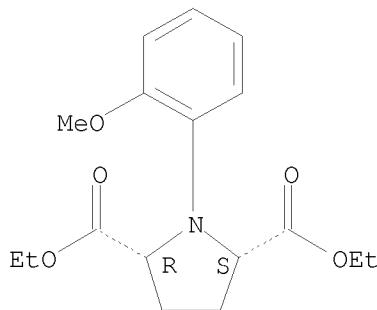
(preparation of heterocycle- and benzene-containing sulfonamide derivs. as

LDL receptor agonists for treatment of hyperlipemia and arteriosclerosis)

RN 850887-29-5 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-(2-methoxyphenyl)-, 2,5-diethyl ester, (2S,5R)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 40 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:963979 CAPLUS

DOCUMENT NUMBER: 143:422221

TITLE: NaBH4-InCl3-Mediated One-Pot Chemo- and Stereoselective Decarboxylative Reduction of  $\alpha$ -Aza gem-Dicarboxylic Esters to Monoalcohols

Halder, Pranab; Ray, Jayanta K.

AUTHOR(S): Department of Chemistry, Indian Institute of Technology, Kharagpur, 721302, India

CORPORATE SOURCE: Organic Letters (2005), 7(20), 4341-4343

SOURCE: CODEN: ORLEF7; ISSN: 1523-7060

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:422221

AB The combination of NaBH4 and a catalytic amount of InCl3 provides a one-pot method for chemo- and stereoselective decarboxylative reduction of gem-dicarboxylic esters to monoalcs. in the presence of the lactam carbonyl in refluxing acetonitrile under inert atmospheric

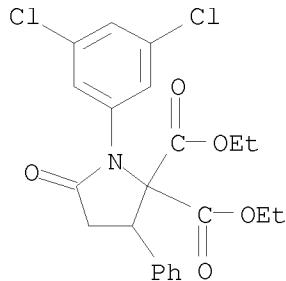
IT 868389-79-1 868389-80-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(NaBH4-InCl3-mediated one-pot chemo- and stereoselective decarboxylative reduction of oxopyrrolidinedicarboxylates to oxopyrrolidinemethanols)

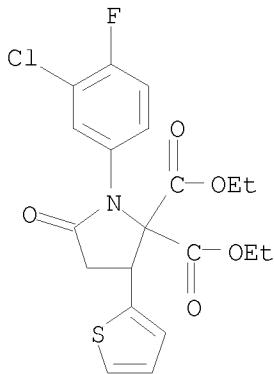
RN 868389-79-1 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-(3,5-dichlorophenyl)-5-oxo-3-phenyl-, 2,2-diethyl ester (CA INDEX NAME)



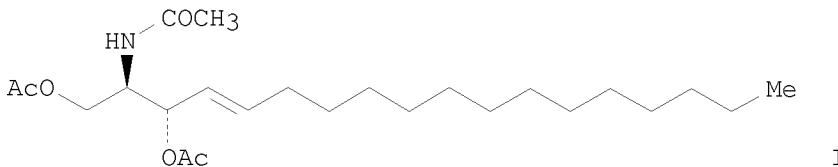
RN 868389-80-4 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-(3-chloro-4-fluorophenyl)-5-oxo-3-(2-thienyl)-, 2,2-diethyl ester (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 41 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:943557 CAPLUS  
 DOCUMENT NUMBER: 144:292438  
 TITLE: Diastereoselective allylation of imines with  $\gamma$ -silyloxyallylstannanes promoted by trimethylsilyl triflate and application to the synthesis of erythro-sphingosine  
 AUTHOR(S): Shimizu, Makoto; Ando, Hiromi; Niwa, Yasuki  
 CORPORATE SOURCE: Department of Chemistry for Materials, Mie University, Mie, 514-8507, Japan  
 SOURCE: Letters in Organic Chemistry (2005), 2(6), 512-514  
 PUBLISHER: Bentham Science Publishers Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 144:292438  
 GI



I

AB Addition of  $\gamma$ -silyloxyallylstannanes to imines in the presence of trimethylsilyl triflate was studied. Allylation of  $\alpha$ -imino ester with (Z)-allylstannane proceeded to give anti-adduct as a major product, which was transformed into N,O,O-triacetyl erythro-sphingosine (I) via appropriate functional group transformations.

IT 879215-07-3P 879215-08-4P 879215-09-5P

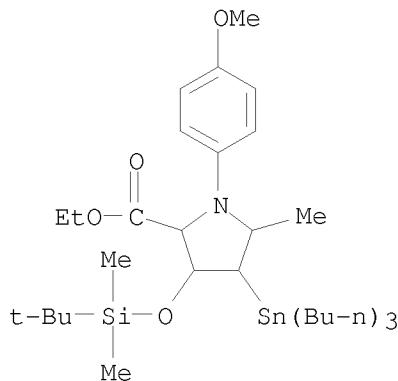
879215-10-8P 879215-11-9P

RL: BYP (Byproduct); PREP (Preparation)

(diastereoselective allylation of imines with  $\gamma$ -silyloxyallylstannanes promoted by trimethylsilyl triflate and application to the synthesis of erythro-sphingosine)

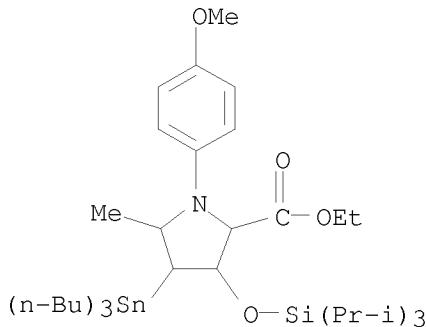
RN 879215-07-3 CAPLUS

CN Proline, 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-(4-methoxyphenyl)-5-methyl-4-(tributylstannyl)-, ethyl ester (CA INDEX NAME)



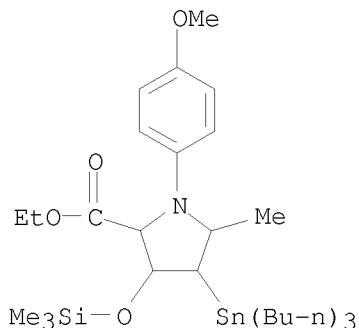
RN 879215-08-4 CAPLUS

CN Proline, 1-(4-methoxyphenyl)-5-methyl-4-(tributylstannylyl)-3-[(tris(1-methylethyl)silyl)oxy]-, ethyl ester (CA INDEX NAME)



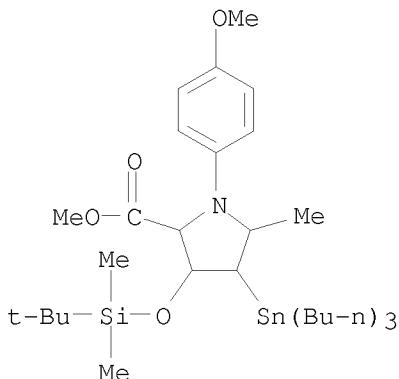
RN 879215-09-5 CAPLUS

CN Proline, 1-(4-methoxyphenyl)-5-methyl-4-(tributylstannylyl)-3-[(trimethylsilyl)oxy]-, ethyl ester (CA INDEX NAME)



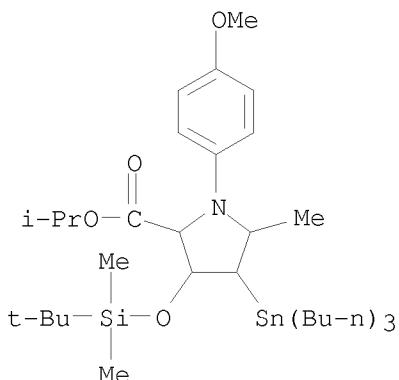
RN 879215-10-8 CAPLUS

CN Proline, 3-[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-(4-methoxyphenyl)-5-methyl-4-(tributylstannylyl)-, methyl ester (CA INDEX NAME)



RN 879215-11-9 CAPLUS

CN Proline, 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-(4-methoxyphenyl)-5-methyl-4-(tributylstannyl)-, 1-methylethyl ester (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 42 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:921231 CAPLUS

DOCUMENT NUMBER: 143:367177

TITLE: Diastereoselective Synthesis of Pyrrolidines via the Yb(OTf)3 Catalyzed Three-Component Reaction of Aldehydes, Amines, and 1,1-Cyclopropanediesters

CARSON, Cheryl A.; KERR, Michael A.

CORPORATE SOURCE: Department of Chemistry, University of Western Ontario, London, ON, N6A 5B7, Can.

SOURCE: Journal of Organic Chemistry (2005), 70(20), 8242-8244  
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:367177

AB Aldimines, generated in situ by the reaction of primary amines or anilines with aldehydes, undergo smooth reaction with various 1,1-cyclopropanediesters in the presence of catalytic Yb(OTf)3. The products are pyrrolidines in which the major diastereomer bears a cis relationship between substituents at the 2- and 5-positions. In most cases the diastereoselectivity is greater than 10:1.

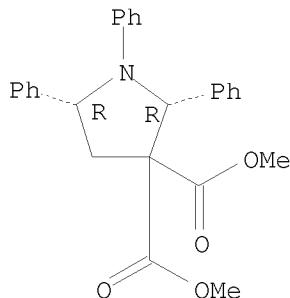
IT 866454-02-6P 866454-06-0P 866454-09-3P  
866454-10-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of N-substituted pyrrolidines via  $\text{Yb}(\text{OTf})_3$  catalyzed  
diastereoselective cycloaddn. of primary amines/anilines, aldehydes,  
and 1,1-cyclopropanediesters)

RN 866454-02-6 CAPLUS

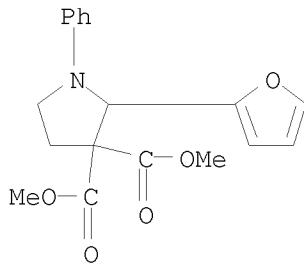
CN 3,3-Pyrrolidinedicarboxylic acid, 1,2,5-triphenyl-, 3,3-dimethyl ester,  
(2R,5R)-rel- (CA INDEX NAME)

Relative stereochemistry.



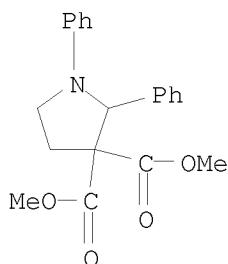
RN 866454-06-0 CAPLUS

CN 3,3-Pyrrolidinedicarboxylic acid, 2-(2-furanyl)-1-phenyl-, 3,3-dimethyl  
ester (CA INDEX NAME)



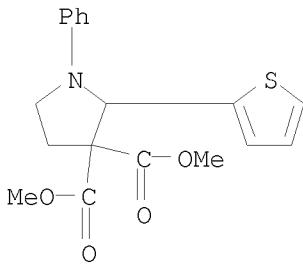
RN 866454-09-3 CAPLUS

CN 3,3-Pyrrolidinedicarboxylic acid, 1,2-diphenyl-, 3,3-dimethyl ester (CA  
INDEX NAME)



RN 866454-10-6 CAPLUS

CN 3,3-Pyrrolidinedicarboxylic acid, 1-phenyl-2-(2-thienyl)-, 3,3-dimethyl  
ester (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 43 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:779160 CAPLUS

DOCUMENT NUMBER: 144:488188

TITLE: New Tandem Reactions of Metal Carbenoids.

Intermolecular Formation of Azomethine Ylide from Methyl 2-Diazo-2-phenylacetate and Schiff Base:

Intramolecular 1,3-Dipolar Cycloaddition

AUTHOR(S): Khlebnikov, A. F.; Novikov, M. S.; Bespokoev, A. A.; Kostikov, R. R.; Kopf, J.; Starikova, Z. A.; Antipin, M. Yu.

CORPORATE SOURCE: St. Petersburg State University, St. Petersburg, 198504, Russia

SOURCE: Russian Journal of Organic Chemistry (2005), 41(6), 922-932

CODEN: RJOCEQ; ISSN: 1070-4280

PUBLISHER: Pleiades Publishing, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:488188

AB Rhodium acetate-catalyzed decomposition of Me 2-diazo-2-phenylacetate in the presence of substituted N-methylbenzylideneamines possessing an activated alkenyl fragment (dipolarophile) in the side chain gives products of intramol. cycloaddn. of intermediate Z,E- and E,Z-azomethine ylides. The cycloaddn. is regioselective, and the products are hexahydrochromeno[4,3-b]pyrrole derivs. The stereoselectivity of the process depends on the temperature. In the temperature range from 20 to 80°C, the major stereoisomer is that with cis junction of the tetrahydropyran and pyrrolidine rings. N-Phenylazomethine ylides generated from Me 2-diazo-2-phenylacetate and alkyl 4-[2-(phenyliminomethyl)phenoxy]-2-butenoates at 40°C undergo cyclization to aziridines at a higher rate, as compared to the rate of cycloaddn. to the internal dipolarophile. N-Phenylazomethine ylides generated by thermolysis of the corresponding aziridine or by the "deprotonation" method react with equal regio- and stereoselectivity to give intramol. cycloaddn. products, hexahydrochromeno[4,3-b]pyrrole derivs. with trans-fused tetrahydropyran and pyrrolidine rings. Anal. of the exptl. and calcn. data suggests preference of the endo transition state in the cycloaddn. of the examined azomethine ylides.

IT 887487-85-6P

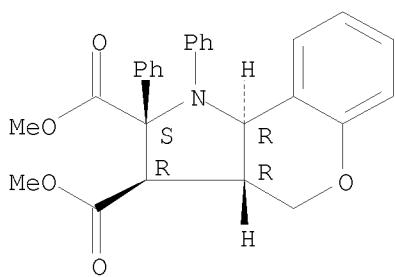
RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(crystallog.; regio- and stereoselective intramol. 1,3-dipolar cycloaddn. of azomethine ylide from Me 2-diazo-2-phenylacetate and Schiff base)

RN 887487-85-6 CAPLUS

CN [1]Benzopyrano[4,3-b]pyrrole-2,3-dicarboxylic acid, 1,2,3,3a,4,9b-hexahydro-1,2-diphenyl-, 2,3-dimethyl ester, (2R,3S,3aS,9bS)-rel- (CA INDEX NAME)

Relative stereochemistry.



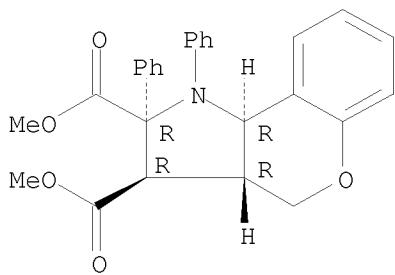
IT 887487-87-8P

RL: BYP (Byproduct); PUR (Purification or recovery); PREP (Preparation)  
(regio- and stereoselective intramol. 1,3-dipolar cycloaddn. of  
azomethine ylide from Me 2-diazo-2-phenylacetate and Schiff base)

RN 887487-87-8 CAPLUS

CN [1]Benzopyrano[4,3-b]pyrrole-2,3-dicarboxylic acid, 1,2,3,3a,4,9b-hexahydro-1,2-diphenyl-, 2,3-dimethyl ester, (2R,3R,3aR,9bR)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 44 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:618408 CAPLUS

DOCUMENT NUMBER: 143:386609

TITLE: Proximity effects: the observation by <sup>1</sup>H NMR of steric compression of the methano bridge protons of polycyclic norbornanes possessing adjacent carbon, oxygen and nitrogen bridges

AUTHOR(S): Margetic, Davor; Johnston, Martin R.; Warrener, Ronald N.; Butler, Douglas N.

CORPORATE SOURCE: Centre for Molecular Architecture, Central Queensland University, Queensland, 4701, Australia

SOURCE: International Electronic Conferences on Synthetic Organic Chemistry, 5th, 6th, Sept. 1-30, 2001 and 2002 [and] 7th, 8th, Nov. 1-30, 2003 and 2004 (2004), 1420-1428. Editor(s): Seijas, Julio A. Molecular Diversity Preservation International: Basel, Switz.

CODEN: 69GTCO

DOCUMENT TYPE: Conference; (computer optical disk)

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:386609

AB Proximity effects of neighboring heteroatom bridges (oxygen, nitrogen)

cause steric compression shifts in the 1H NMR chemical shifts of the bridge methano protons in fused norbornanes. This observation provides a simple 2-dimensional NMR method for elucidating the stereochem. outcome of cycloaddn. reactions that produce fused norbornane structures.

IT 866625-96-9

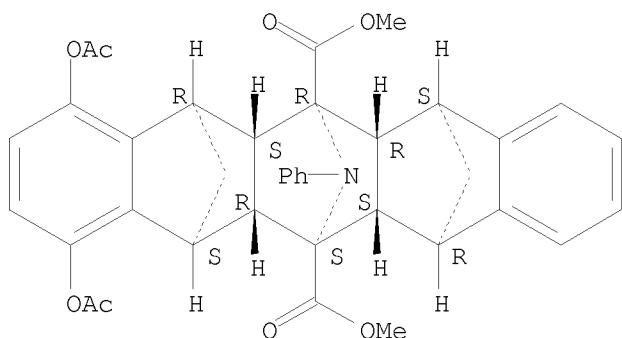
RL: PRP (Properties)

(proximity effects and 1H NMR observations of steric compression of methano bridge protons of polycyclic norbornanes possessing adjacent carbon, oxygen and nitrogen bridges)

RN 866625-96-9 CAPLUS

CN 5,14:7,12-Dimethanopentacen-6,13-imine-6,13-dicarboxylic acid, 1,4-bis(acetoxy)-5,5a,6a,7,12,12a,13a,14-octahydro-16-phenyl-, dimethyl ester, (5R,5aS,6R,6aR,7S,12R,12aS,13S,13aR,14S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 45 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:449667 CAPLUS

DOCUMENT NUMBER: 142:481953

TITLE: Preparation of pyridylpyrrolidinedicarboxamides, asymmetric acylation catalysts containing them, and preparation of optically active compounds using them

INVENTOR(S): Kawabata, Takeo

PATENT ASSIGNEE(S): Tokuyama Corp., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.

CODEN: JKXXAF

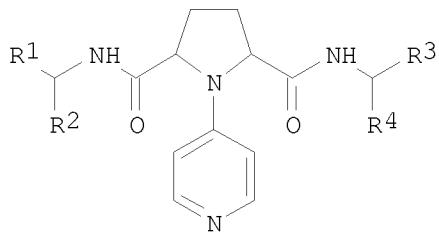
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005132746	A	20050526	JP 2003-368239	20031029
PRIORITY APPLN. INFO.:			JP 2003-368239	20031029
OTHER SOURCE(S):	MARPAT	142:481953		
GI				



I

AB The carboxamides I [R1, R3 = H, C1-6 alkoxy carbonyl; R2, R4 = H, C $\leq$ 10 aromatic hydrocarbyl, (C $\leq$ 10 aromatic heterocycle-substituted) C $\leq$ 6 alkyl; R1 = R2  $\neq$  H; R3 = R4  $\neq$  H] are prepared by amidation of 1-(4-pyridyl)pyrrolidine-2,5-dicarboxylic acid with H2NCHR1R2 (R1, R2 = same as I) and H2NCHR3R4 (R3, R4 = same as I) using condensing agents. The catalysts comprise I with  $\geq$ 50% optical purity. Meso-1,2-cyclohexanediol was acylated by isobutyric anhydride in the presence of (2S,5S)-1-(4-pyridyl)-2,5-bis[N-[(1S)-1-methoxycarbonyl-2-(3-indolyl)ethyl]carbamoyl]pyrrolidine and 2,4,6-collidine in CHCl3 at 20° for 4 h to give monoester with 73% ee and 85% selectivity.

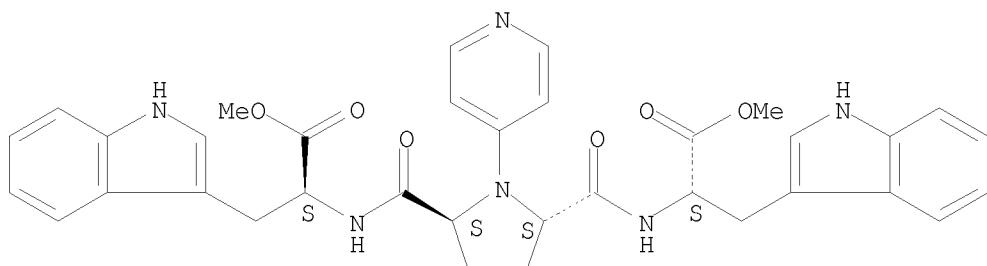
IT 852204-84-3P 852204-85-4P 852204-86-5P  
852204-87-6P 852204-88-7P 852204-89-8P  
852204-90-1P

RL: CAT (Catalyst use); SPN (Synthetic preparation); PREP (Preparation);  
USES (Uses)  
(preparation of optically active pyridylpyrrolidinedicarboxamides as asym.  
acylation catalysts)

RN 852204-84-3 CAPLUS

CN L-Tryptophan, N,N'-[[(2S,5S)-1-(4-pyridinyl)-2,5-pyrrolidinediyl]dicarbonyl]bis-, dimethyl ester (9CI) (CA INDEX NAME)

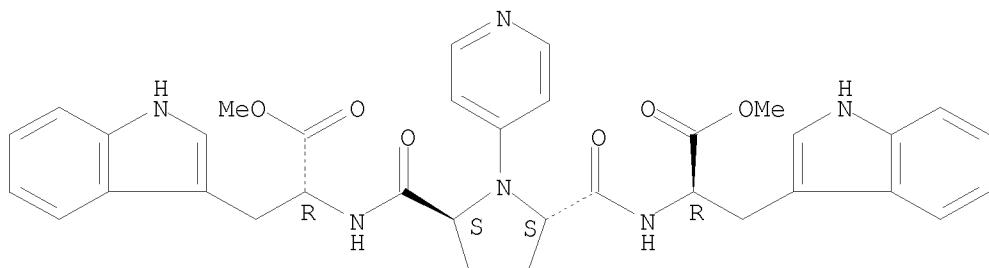
Absolute stereochemistry. Rotation (-).



RN 852204-85-4 CAPLUS

CN D-Tryptophan, N,N'-[[(2S,5S)-1-(4-pyridinyl)-2,5-pyrrolidinediyl]dicarbonyl]bis-, dimethyl ester (9CI) (CA INDEX NAME)

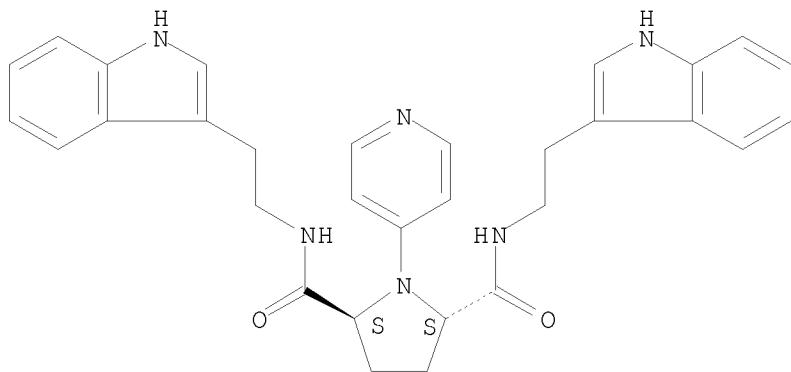
Absolute stereochemistry. Rotation (-).



RN 852204-86-5 CAPLUS

CN 2,5-Pyrrolidinedicarboxamide, N2,N5-bis[2-(1H-indol-3-yl)ethyl]-1-(4-pyridinyl)-, (2S,5S)- (CA INDEX NAME)

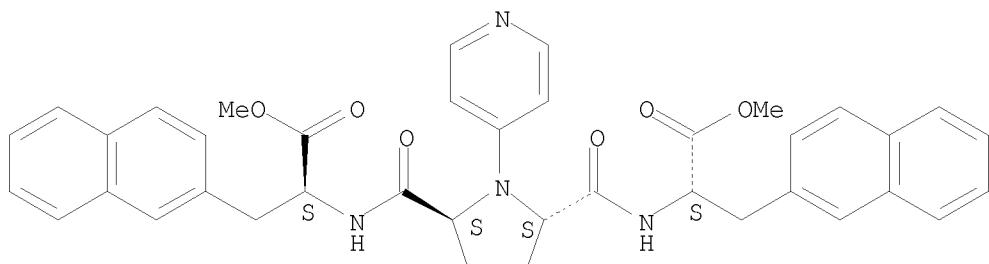
Absolute stereochemistry. Rotation (+).



RN 852204-87-6 CAPLUS

CN 2-Naphthalenepropanoic acid,  $\alpha,\alpha'$ -[[(2S,5S)-1-(4-pyridinyl)-2,5-pyrrolidinediyl]bis(carbonylimino)]bis-, dimethyl ester, ( $\alpha S,\alpha' S$ )- (9CI) (CA INDEX NAME)

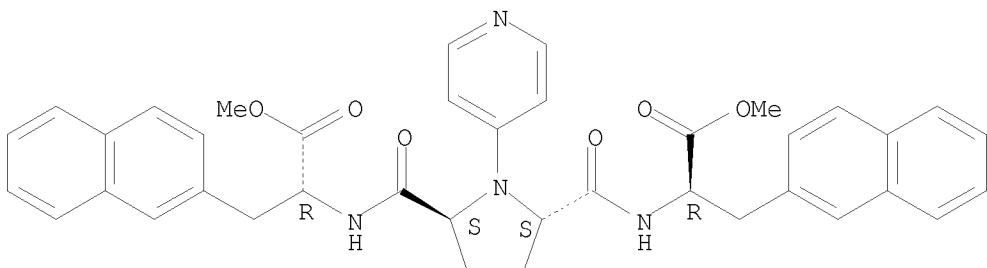
Absolute stereochemistry. Rotation (+).



RN 852204-88-7 CAPLUS

CN 2-Naphthalenepropanoic acid,  $\alpha,\alpha'$ -[[(2S,5S)-1-(4-pyridinyl)-2,5-pyrrolidinediyl]bis(carbonylimino)]bis-, dimethyl ester, ( $\alpha R,\alpha' R$ )- (9CI) (CA INDEX NAME)

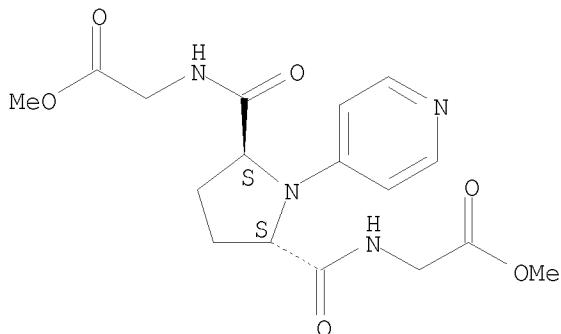
Absolute stereochemistry. Rotation (-).



RN 852204-89-8 CAPLUS

CN Glycine, N,N'-[[(2S,5S)-1-(4-pyridinyl)-2,5-pyrrolidinediyl]dicarbonyl]bis-, dimethyl ester (9CI) (CA INDEX NAME)

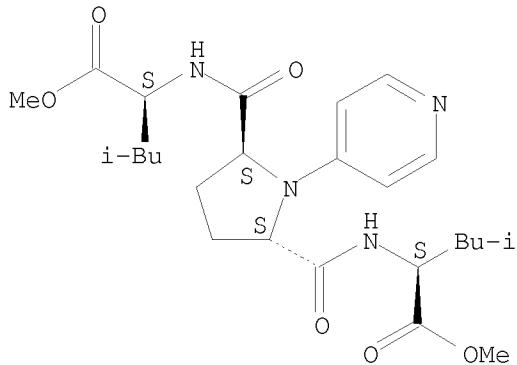
Absolute stereochemistry. Rotation (-).



RN 852204-90-1 CAPLUS

CN L-Leucine, N,N'-[[(2S,5S)-1-(4-pyridinyl)-2,5-pyrrolidinediyl]dicarbonyl]bis-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

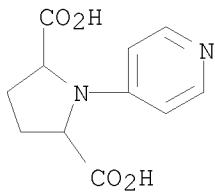


IT 852204-92-3

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of optically active pyridylpyrrolidinedicarboxamides as asym. acylation catalysts)

RN 852204-92-3 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-pyridinyl)- (CA INDEX NAME)



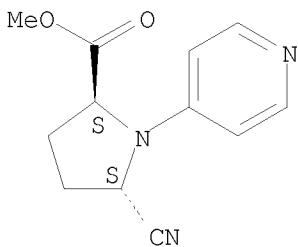
IT 852204-80-9P 852204-81-0P 852204-82-1P  
 852204-83-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of optically active pyridylpyrrolidinedicarboxamides as asym. acylation catalysts)

RN 852204-80-9 CAPLUS

CN L-Proline, 5-cyano-1-(4-pyridinyl)-, methyl ester, (5S)- (CA INDEX NAME)

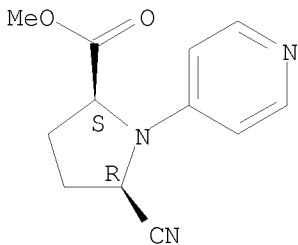
Absolute stereochemistry. Rotation (-).



RN 852204-81-0 CAPLUS

CN L-Proline, 5-cyano-1-(4-pyridinyl)-, methyl ester, (5R)- (CA INDEX NAME)

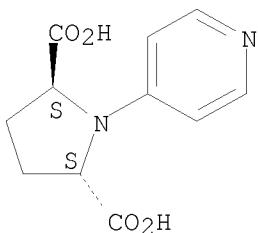
Absolute stereochemistry. Rotation (-).



RN 852204-82-1 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-pyridinyl)-, hydrochloride (1:1), (2S,5S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

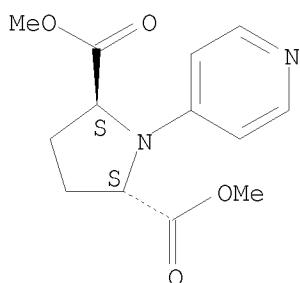


● HCl

RN 852204-83-2 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-(4-pyridinyl)-, 2,5-dimethyl ester, (2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 46 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:369273 CAPLUS

DOCUMENT NUMBER: 142:430299

TITLE: Preparation of novel piperidine and cyclohexanecarbonitrile derivatives effective in enhancing LDL receptor manifestation

INVENTOR(S): Ban, Hitoshi; Ohnuma, Satoshi; Tsuboya, Norie; Asano, Shigehiro

PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan

SOURCE: PCT Int. Appl., 209 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

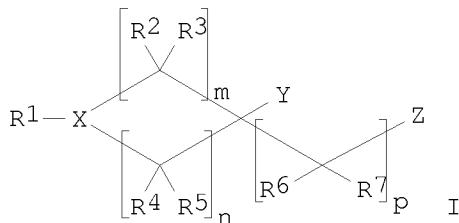
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037269	A1	20050428	WO 2004-JP15773	20041019
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,				

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG  
 EP 1679069 A1 20060712 EP 2004-792910 20041019  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK  
 US 20070078120 A1 20070405 US 2006-576581 20060420  
 PRIORITY APPLN. INFO.: JP 2003-361256 A 20031021  
 WO 2004-JP15773 W 20041019  
 OTHER SOURCE(S): MARPAT 142:430299  
 GI



AB Drugs for enhancing LDL receptor manifestation contains compds. represented by the following formula (I), prodrugs thereof, or pharmaceutically acceptable salts of either [m, n, p = 0-4, provided that  $3 \leq m+n \leq 8$ ; X = N, each (un)substituted CH; Y = each (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, or aromatic group, COY; R1 = H, each (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, 3- to 8-membered saturated heterocyclyl containing one (un)substituted NH or O, aromatic group, COR14; R14 = each (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, or aromatic group; R2-R7 = H, OH, each (un)substituted alkyl, alkoxy, alkoxy carbonyl, aralkyl, heteroarylalkyl, aralkyloxy, or heteroarylalkyloxy; or one or a plural combination of R2 and R3, R4 and R5, or R6 and R7 = oxo; or R2 and R4 together = alkylene; two of R2-R5 are on the adjacent carbon atom to form a double bond; Z = H, OH, CO2H, cyano, phthalimido, halo, each (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, or aromatic group, etc.] as active ingredients. These compds. are effective in enhancing low d. lipoprotein (LDL) receptor manifestation and lowering blood concentration of LDL cholesterol and are useful as therapeutic agents for treating hyperlipemia and arteriosclerosis. Thus, 0.019 mL benzyl bromide was added to a suspension of 40 mg 4-(3-methoxyphenyl)-1,4'-bipiperidine-4-carbonitrile dihydrochloride and 92.6 mg K2CO3 in 1.0 mL DMF under ice-cooling, and the resulting mixture was warmed to room temperature,

stirred overnight, and quenched by adding water to give, after workup and silica gel chromatog., 15.6 mg 1'-benzyl-4-(3-methoxyphenyl)-1,1'-bipiperidine-4-carbonitrile (II). II at 10  $\mu$ M and N-benzyl-4-(3-methoxyphenyl)-1-(pyrimidin-2-yl)piperidine-4-carbothioamide at 3  $\mu$ M enhanced the LDL receptor activity by 135 and 195%, resp.

IT 850887-29-5P, Diethyl cis-1-(2-methoxyphenyl)pyrrolidine-2,5-dicarboxylate

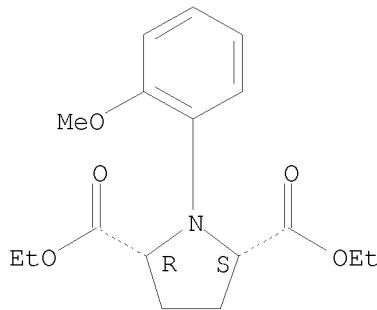
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of novel piperidine and cyclohexanecarbonitrile derivs. as enhancers for LDL receptor manifestation, hypolipidemics, and antiarteriosclerotics)

RN 850887-29-5 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-(2-methoxyphenyl)-, 2,5-diethyl ester,  
(2S,5R)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 47 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2005:238948 CAPLUS  
DOCUMENT NUMBER: 142:317078  
TITLE: Preparation of pyrrolidine-2-carbonitrile derivatives and their use as inhibitors of dipeptidyl peptidase-IV (DPP-IV)  
INVENTOR(S): Pei, Zhonghua; Li, Xiaofeng; Longenecker, Kenton L.; Sham, Hing L.; Wiedeman, Paul E.  
PATENT ASSIGNEE(S): Abbott Laboratories, USA  
SOURCE: PCT Int. Appl., 182 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023762	A1	20050317	WO 2004-US28886	20040907
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-655428 A 20030904

OTHER SOURCE(S): CASREACT 142:317078; MARPAT 142:317078

AB The invention relates to 1-(5-ROCH<sub>2</sub>-substituted prolyl)pyrrolidine-2-carbonitriles (R is substituted Ph, 2-, 3-, or 4-pyridyl, or 4-quinolyl) or their pharmaceutically-acceptable salts or prodrugs, which inhibit dipeptidyl peptidase IV (DPP-IV) and are useful for the prevention or treatment of diabetes, especially type II diabetes, as well as hyperglycemia, syndrome X, hyperinsulinemia,  $\beta$ -cell failure, obesity, satiety disorders, atherosclerosis, and various immunomodulatory diseases. Thus, (2S)-1-[(5R)-5-[(4-carboxynaphthalen-1-yloxy)methyl]-L-prolyl]pyrrolidine-2-carbonitrile, prepared via N-acylation and etherification reactions, was

evaluated for ability to treat diabetes using an acute oral glucose tolerance test ( $\delta$  AUGC = 7,600 mg/mL/dL at 1.0 mg/kg vs. 9,900 mg/mL/dL for the control).

IT 847942-13-6P

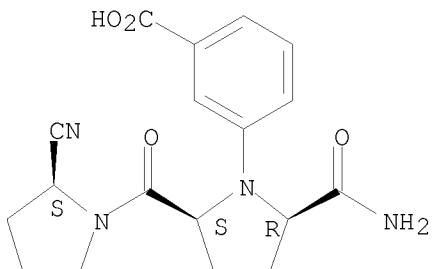
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrrolidinecarbonitrile derivs. as inhibitors of dipeptidyl peptidase-IV)

RN 847942-13-6 CAPLUS

CN Benzoic acid, 3-[(2R,5S)-2-(aminocarbonyl)-5-[(2S)-2-cyano-1-pyrrolidinyl]carbonyl]-1-pyrrolidinyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 48 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:86460 CAPLUS

DOCUMENT NUMBER: 142:328905

TITLE: Structure-based design of potent and selective inhibitors of collagenase-3 (MMP-13)

AUTHOR(S): Kim, Soong-Hoon; Pudzianowski, Andrew T.; Leavitt, Kenneth J.; Barbosa, Joseph; McDonnell, Patricia A.; Metzler, William J.; Rankin, Bruce M.; Liu, Richard; Vaccaro, Wayne; Pitts, William

CORPORATE SOURCE: Bristol Myers Squibb Co., Pharmaceutical Research Institute, Princeton, NJ, 08560, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(4), 1101-1106

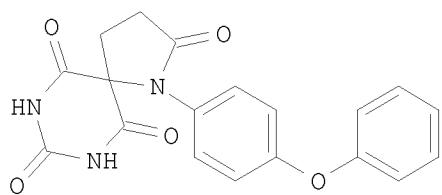
PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 142:328905

GI



I

AB Computer aided drug design led to a new class of spiro-barbiturates (e.g., I, MMP-13 Ki = 4.7 nM) that are potent inhibitors of MMP-13.

IT 848773-40-0P 848773-41-1P 848773-42-2P

848773-48-8P 848773-49-9P 848773-50-2P

848773-51-3P 848773-52-4P 848773-53-5P

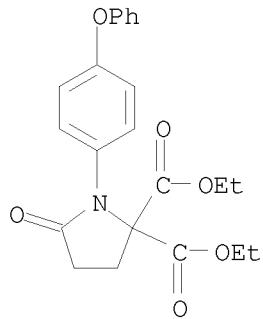
848773-54-6P 848773-55-7P 848773-56-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(Structure-based design of potent and selective inhibitors of collagenase-3)

RN 848773-40-0 CAPLUS

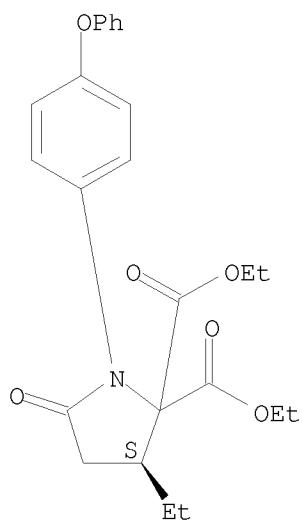
CN 2,2-Pyrrolidinedicarboxylic acid, 5-oxo-1-(4-phenoxyphenyl)-, 2,2-diethyl ester (CA INDEX NAME)



RN 848773-41-1 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 3-ethyl-5-oxo-1-(4-phenoxyphenyl)-, 2,2-diethyl ester, (3S)- (CA INDEX NAME)

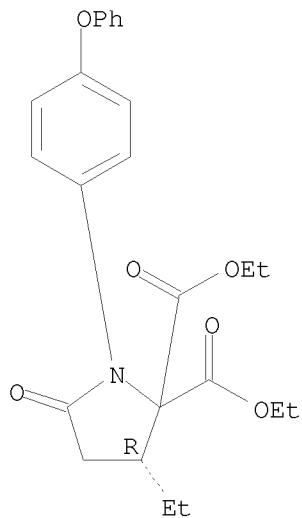
Absolute stereochemistry.



RN 848773-42-2 CAPLUS

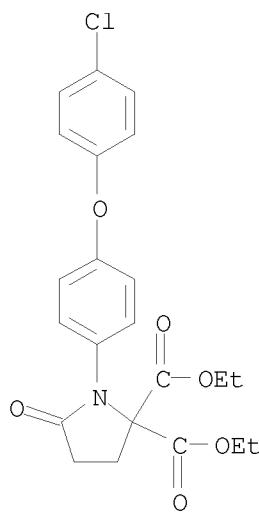
CN 2,2-Pyrrolidinedicarboxylic acid, 3-ethyl-5-oxo-1-(4-phenoxyphenyl)-, 2,2-diethyl ester, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



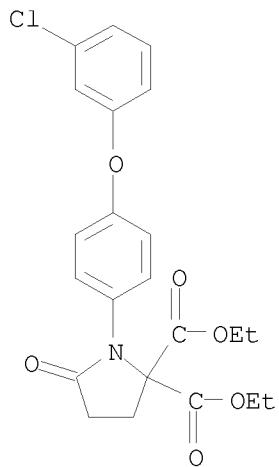
RN 848773-48-8 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-[4-(4-chlorophenoxy)phenyl]-5-oxo-, 2,2-diethyl ester (CA INDEX NAME)



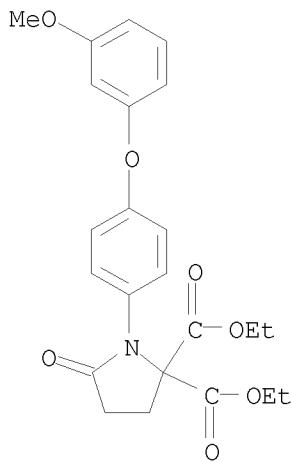
RN 848773-49-9 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-[4-(3-chlorophenoxy)phenyl]-5-oxo-,  
2,2-diethyl ester (CA INDEX NAME)



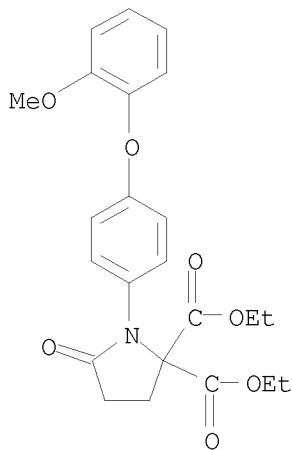
RN 848773-50-2 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-[4-(3-methoxyphenoxy)phenyl]-5-oxo-,  
2,2-diethyl ester (CA INDEX NAME)



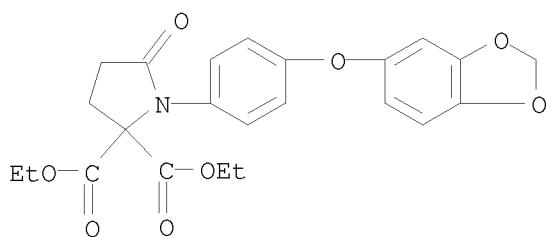
RN 848773-51-3 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-[4-(2-methoxyphenoxy)phenyl]-5-oxo-, 2,2-diethyl ester (CA INDEX NAME)



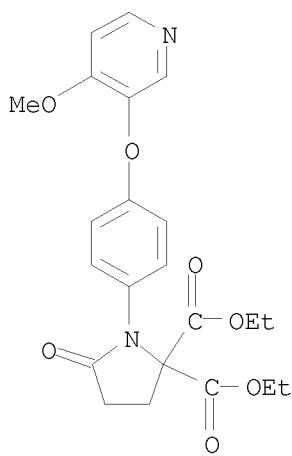
RN 848773-52-4 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-[4-(1,3-benzodioxol-5-yloxy)phenyl]-5-oxo-, 2,2-diethyl ester (CA INDEX NAME)



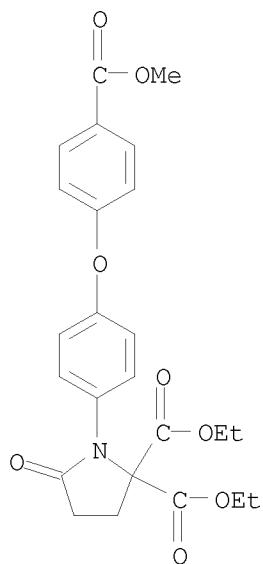
RN 848773-53-5 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-[4-[(4-methoxy-3-pyridinyl)oxy]phenyl]-5-oxo-, 2,2-diethyl ester (CA INDEX NAME)



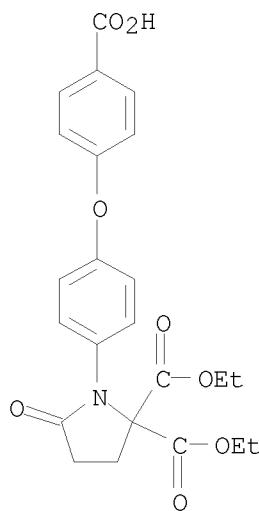
RN 848773-54-6 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-[4-[4-(methoxycarbonyl)phenoxy]phenyl]-5-oxo-, 2,2-diethyl ester (CA INDEX NAME)



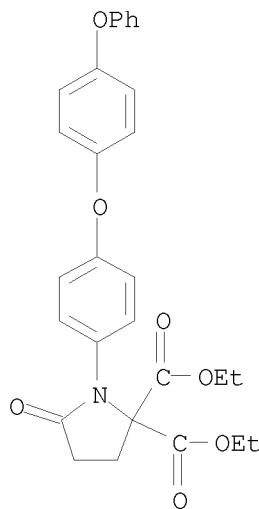
RN 848773-55-7 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 1-[4-[4-(4-carboxyphenoxy)phenoxy]phenyl]-5-oxo-, 2,2-diethyl ester (CA INDEX NAME)



RN 848773-56-8 CAPLUS

CN 2,2-Pyrrolidinedicarboxylic acid, 5-oxo-1-[4-(4-phenoxyphenoxy)phenyl]-, 2,2-diethyl ester (CA INDEX NAME)



REFERENCE COUNT:

39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 49 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:85523 CAPLUS

DOCUMENT NUMBER: 142:336502

TITLE: Diastereoselective Synthesis of Pyrrolidines Using a Nitrone/Cyclopropane Cycloaddition: Synthesis of the Tetracyclic Core of Nakadomarin A

AUTHOR(S): Young, Ian S.; Williams, Justin L.; Kerr, Michael A.  
CORPORATE SOURCE: Department of Chemistry, The University of Western Ontario, London, ON, N6A 5B7, Can.

SOURCE: Organic Letters (2005), 7(5), 953-955  
CODEN: ORLEF7; ISSN: 1523-7060

PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal

LANGUAGE: English  
OTHER SOURCE(S): CASREACT 142:336502  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The synthesis of the tetracyclic core, I, of nakadomarin A is described. The core contains all the heterocycles and the required stereocenters found in the natural product and provides a promising route to the target itself. The strategy utilizes a general, diastereoselective pyrrolidine synthesis that proceeds via a homo 3 + 2 dipolar cycloaddn. For example, the intermediate amino alc. II was generated by cleavage of the N-O bond of the oxazine III and recyclization of II gave a tricyclic pyrrolidine which was subsequently transformed into I. The scope of this methodol. is also described.

IT 848586-89-0P 848586-91-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

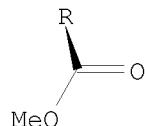
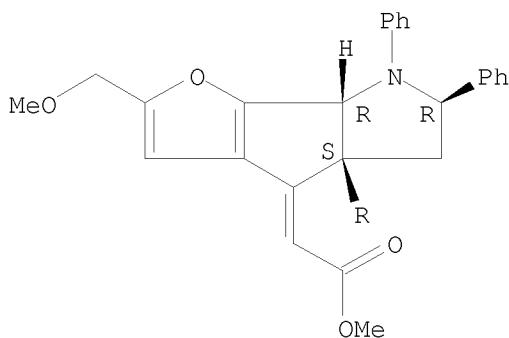
(diastereoselective synthesis of pyrrolidines via nitrone/cyclopropane cycloaddn. and application to synthesis of tetracyclic core of nakadomarin A)

RN 848586-89-0 CAPLUS

CN Furo[3',2':4,5]cyclopenta[1,2-b]pyrrole-4a(4H)-carboxylic acid, 5,6,7,7a-tetrahydro-2-(methoxymethyl)-4-(2-methoxy-2-oxoethylidene)-6,7-diphenyl-, methyl ester, (4aR,6S,7aS)-rel- (CA INDEX NAME)

Relative stereochemistry.

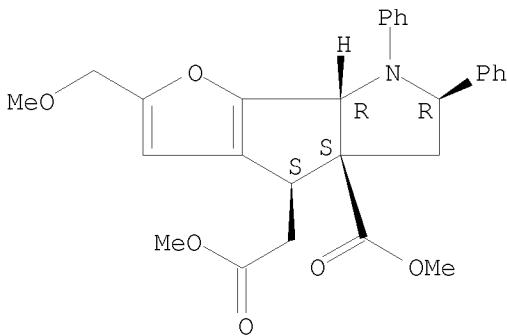
Double bond geometry unknown.



RN 848586-91-4 CAPLUS

CN Furo[3',2':4,5]cyclopenta[1,2-b]pyrrole-4(4H)-acetic acid, 5,6,7,7a-tetrahydro-4a-(methoxycarbonyl)-2-(methoxymethyl)-6,7-diphenyl-, methyl ester, (4R,4aR,6S,7aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT.

L3 ANSWER 50 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:76721 CAPLUS

DOCUMENT NUMBER: 142:430075

**TITLE:** Synthesis of ethyl cis- and trans-4-chloro-5-oxo-1,2-diphenyl-pyrrolidine-2-carboxylate

AUTHOR(S): Martirosyan, A. O.; Hovhannesyan, V. E.; Gasparyan, S. P.; Karapetyan, A. A.; Panosyan, G. A.; Martirosyan, V. O.

CORPORATE SOURCE: A. L. Mndzhoyan Institute of Fine Chemistry, Armenian Republic National Academy of Sciences, Yerevan, 375014, Armenia

SOURCE: Chemistry of Heterocyclic Compounds (New York, NY, United States) (2004), 40(8), 1007-1008

PUBLISHER: CODEN: CHCCAL; ISSN: 0009-3122  
Springer Science+Business Medi

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREAC

AB Et cis- and trans-4-chloro-5-oxo-1,2-di

were synthesized by the cyclization of Et N-( $\alpha$ , $\beta$ -dichloropropionyl)-N-phenyl- $\alpha$ -aminophenylacetate.

IT 850836-21-4P 850836-22-5P

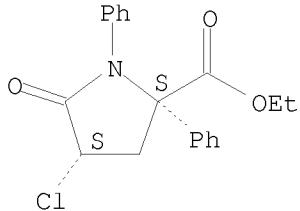
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of Et *cis*- and *trans*-4-chloro-5-oxo-1,2-diphenyl-pyrrolidine-2-carboxylate by cyclization of Et N-( $\alpha$ , $\beta$ -dichloropropionyl)-N-phenyl- $\alpha$ -aminophenylacetate)

RN 850836-21-4 CAPLUS

CN D-Proline, 4-chloro-5-oxo-1,2-diphenyl-, ethyl ester, (4S)-rel- (CA INDEX  
NAME)

## Relative stereochemistry.

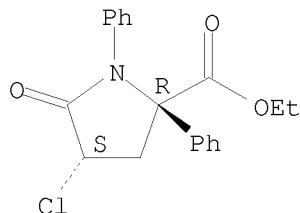


RN 850836-22-5 CAPLUS

CN D-Proline, 4-chloro-5-oxo-1,2-diphenyl-, ethyl ester, (4R)-rel- (9CI) (CA)

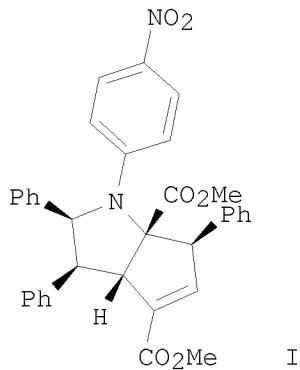
INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

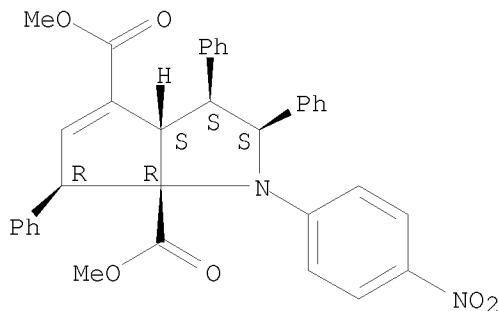
L3 ANSWER 51 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2005:8762 CAPLUS  
DOCUMENT NUMBER: 142:219110  
TITLE: Stereoselective synthesis of bicyclic pyrrolidines by a rhodium-catalyzed cascade process  
AUTHOR(S): Yan, Ming; Jacobsen, Neil; Hu, Wenhao; Gronenberg, Luisa S.; Doyle, Michael P.; Colyer, John T.; Bykowski, Darren  
CORPORATE SOURCE: Department of Chemistry, University of Maryland, College Park, MD, 20742, USA  
SOURCE: Angewandte Chemie, International Edition (2004), 43(48), 6713-6716  
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 142:219110  
GI



AB Multiple C-C bonds were formed in an unprecedented reaction of an ylide with an excess of a rhodium-stabilized carbene. The cascade cyclization of the intermediates, formed from the three components, gave bicyclic pyrrolidines, e.g., I, with excellent diastereoselectivity.  
IT 844437-12-3P  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (stereoselective preparation and crystal structure of N-(nitrophenyl)triphenylazabicyclooctenedicarboxylate via rhodium-catalyzed stereoselective cyclization of N-

(benzylidene)nitroaniline with diazo(phenyl)butenoate  
 RN 844437-12-3 CAPLUS  
 CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-1-(4-nitrophenyl)-2,3,6-triphenyl-, 4,6a-dimethyl ester, (2S,3S,3aS,6R,6aR)-(CA INDEX NAME)

Absolute stereochemistry.

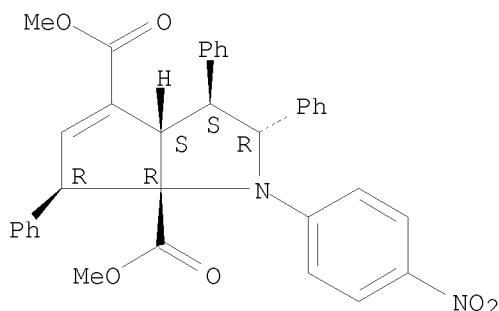


IT 844437-13-4P 844437-14-5P 844437-15-6P  
 844437-16-7P 844437-17-8P 844437-18-9P  
 844437-19-0P 844437-20-3P 844437-21-4P  
 844437-22-5P 844437-23-6P 844437-24-7P  
 844437-25-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (stereoselective preparation of tetra(aryl)azabicyclooctenedicarboxylates  
 via rhodium-catalyzed stereoselective cyclization of  
 N-(benzylidene)anilines with diazo(phenyl)butenoate)

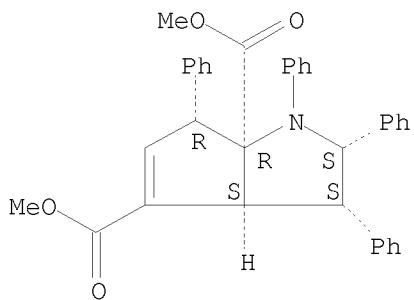
RN 844437-13-4 CAPLUS  
 CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-1-(4-nitrophenyl)-2,3,6-triphenyl-, 4,6a-dimethyl ester, (2R,3S,3aS,6R,6aR)-(CA INDEX NAME)

Absolute stereochemistry.



RN 844437-14-5 CAPLUS  
 CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-1,2,3,6-tetraphenyl-, 4,6a-dimethyl ester, (2S,3S,3aS,6R,6aR)-(CA INDEX NAME)

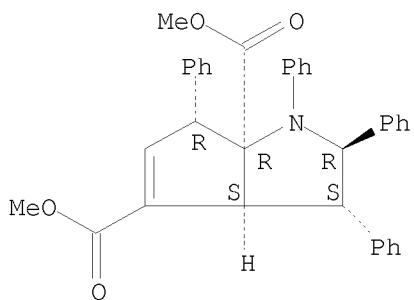
Absolute stereochemistry.



RN 844437-15-6 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-1,2,3,6-tetraphenyl-, 4,6a-dimethyl ester, (2R,3S,3aS,6R,6aR)- (CA INDEX NAME)

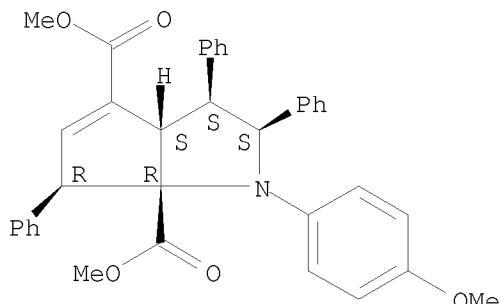
Absolute stereochemistry.



RN 844437-16-7 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-1-(4-methoxyphenyl)-2,3,6-triphenyl-, 4,6a-dimethyl ester, (2S,3S,3aS,6R,6aR)- (CA INDEX NAME)

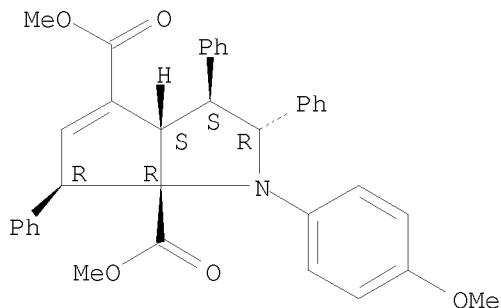
Absolute stereochemistry.



RN 844437-17-8 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-1-(4-methoxyphenyl)-2,3,6-triphenyl-, 4,6a-dimethyl ester, (2R,3S,3aS,6R,6aR)- (CA INDEX NAME)

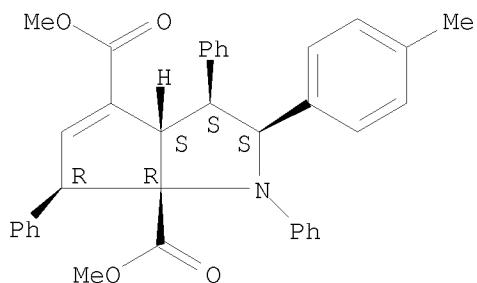
Absolute stereochemistry.



RN 844437-18-9 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-2-(4-methylphenyl)-1,3,6-triphenyl-, 4,6a-dimethyl ester, (2S,3S,3aS,6R,6aR)- (CA INDEX NAME)

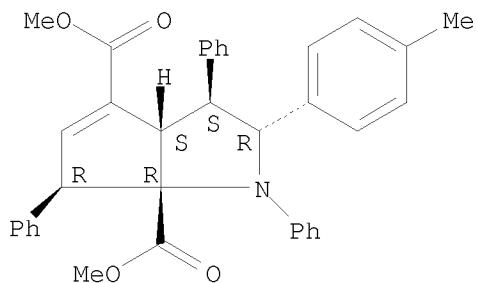
Absolute stereochemistry.



RN 844437-19-0 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-2-(4-methylphenyl)-1,3,6-triphenyl-, 4,6a-dimethyl ester, (2R,3S,3aS,6R,6aR)- (CA INDEX NAME)

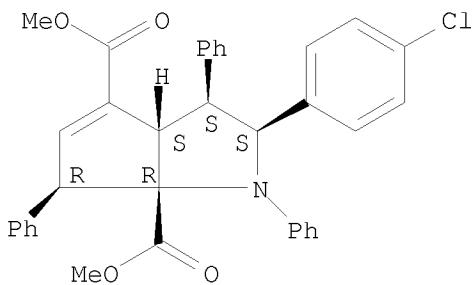
Absolute stereochemistry.



RN 844437-20-3 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2-(4-chlorophenyl)-2,3,3a,6-tetrahydro-1,3,6-triphenyl-, 4,6a-dimethyl ester, (2S,3S,3aS,6R,6aR)- (CA INDEX NAME)

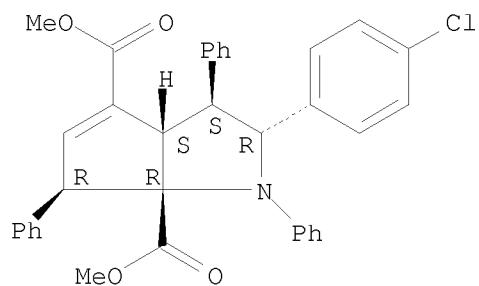
Absolute stereochemistry.



RN 844437-21-4 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2-(4-chlorophenyl)-2,3,3a,6-tetrahydro-1,3,6-triphenyl-, 4,6a-dimethyl ester, (2R,3S,3aS,6R,6aR)- (CA INDEX NAME)

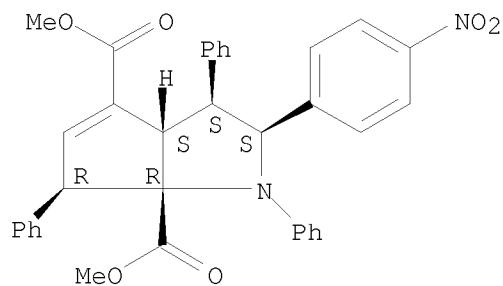
Absolute stereochemistry.



RN 844437-22-5 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-2-(4-nitrophenyl)-1,3,6-triphenyl-, 4,6a-dimethyl ester, (2S,3S,3aS,6R,6aR)- (CA INDEX NAME)

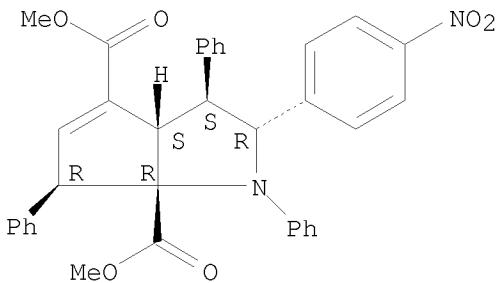
Absolute stereochemistry.



RN 844437-23-6 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-2-(4-nitrophenyl)-1,3,6-triphenyl-, 4,6a-dimethyl ester, (2R,3S,3aS,6R,6aR)- (CA INDEX NAME)

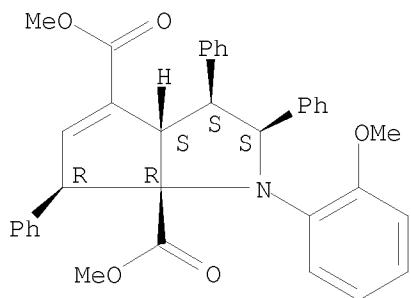
Absolute stereochemistry.



RN 844437-24-7 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-1-(2-methoxyphenyl)-2,3,6-triphenyl-, 4,6a-dimethyl ester, (2S,3S,3aS,6R,6aR)-(CA INDEX NAME)

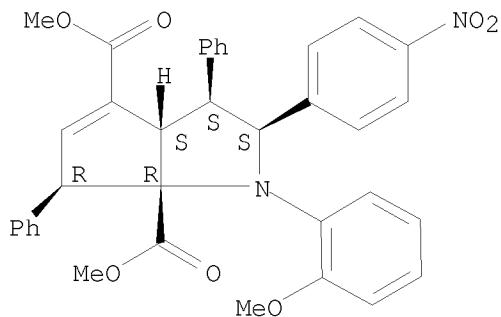
Absolute stereochemistry.



RN 844437-25-8 CAPLUS

CN Cyclopenta[b]pyrrole-4,6a(1H)-dicarboxylic acid, 2,3,3a,6-tetrahydro-1-(2-methoxyphenyl)-2-(4-nitrophenyl)-3,6-diphenyl-, 4,6a-dimethyl ester, (2S,3S,3aS,6R,6aR)-(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

33

THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

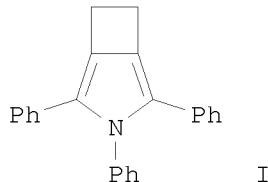
L3 ANSWER 52 OF 73 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1066156 CAPLUS

DOCUMENT NUMBER: 142:155758

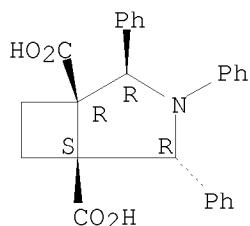
TITLE: 2,3,4-Triphenyl-3-azabicyclo[3.2.0]hepta-1,4-diene - facile ring-opening by electrophiles and novel reactions with dimethyl acetylenedicarboxylate

AUTHOR(S): Matsumoto, Kiyoshi; Goto, Sadahito; Hayashi, Naoto;  
 Iida, Hirokazu; Uchida, Takane; Kakehi, Akikazu  
 CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Chiba Institute of  
 Science, Chiba, 288-0025, Japan  
 SOURCE: European Journal of Organic Chemistry (2004), (22),  
 4667-4671  
 CODEN: EJOCFK; ISSN: 1434-193X  
 PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 142:155758  
 GI



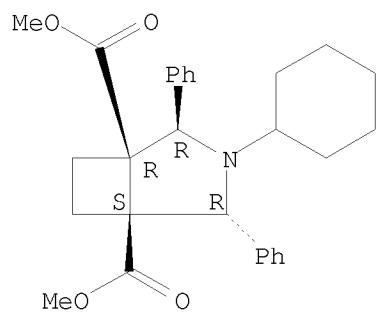
AB A 3-azabicyclo[3.2.0]hepta-1,4-diene I with no substituent in the cyclobutene moiety has been prepared. I underwent extremely facile electrophilic attack at the  $\beta$ -position to give the ring-opened products, probably by a retro-Friedel-Crafts process. I reacted with di-Me acetylenedicarboxylate to afford the corresponding azepine.  
 IT 828917-31-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of azabicycloheptanedicarboxylic acids via hydrolysis of azabicycloheptanedicarboxylates)  
 RN 828917-31-3 CAPLUS  
 CN 3-Azabicyclo[3.2.0]heptane-1,5-dicarboxylic acid, 2,3,4-triphenyl-, (1R,2R,4R,5S)-rel- (CA INDEX NAME)

Relative stereochemistry.



IT 828917-30-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (stereoselective preparation of azabicycloheptanedicarboxylates via stereoselective dipolar cycloaddn. of aziridines to cyclobutenedicarboxylate)  
 RN 828917-30-2 CAPLUS  
 CN 3-Azabicyclo[3.2.0]heptane-1,5-dicarboxylic acid, 3-cyclohexyl-2,4-diphenyl-, 1,5-dimethyl ester, (1S,2S,4S,5R)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

35

THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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